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Vol. XXI, No. 5 MAY, 1932

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 80th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN TORONTO, CANADA, IN 1932—August 22nd–27th, Royal York Hotel, Headquarters, R. B. J. Stanbury, 43 Victoria St., Toronto 2, Canada, Local Secretary.

The 1932 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Toronto.

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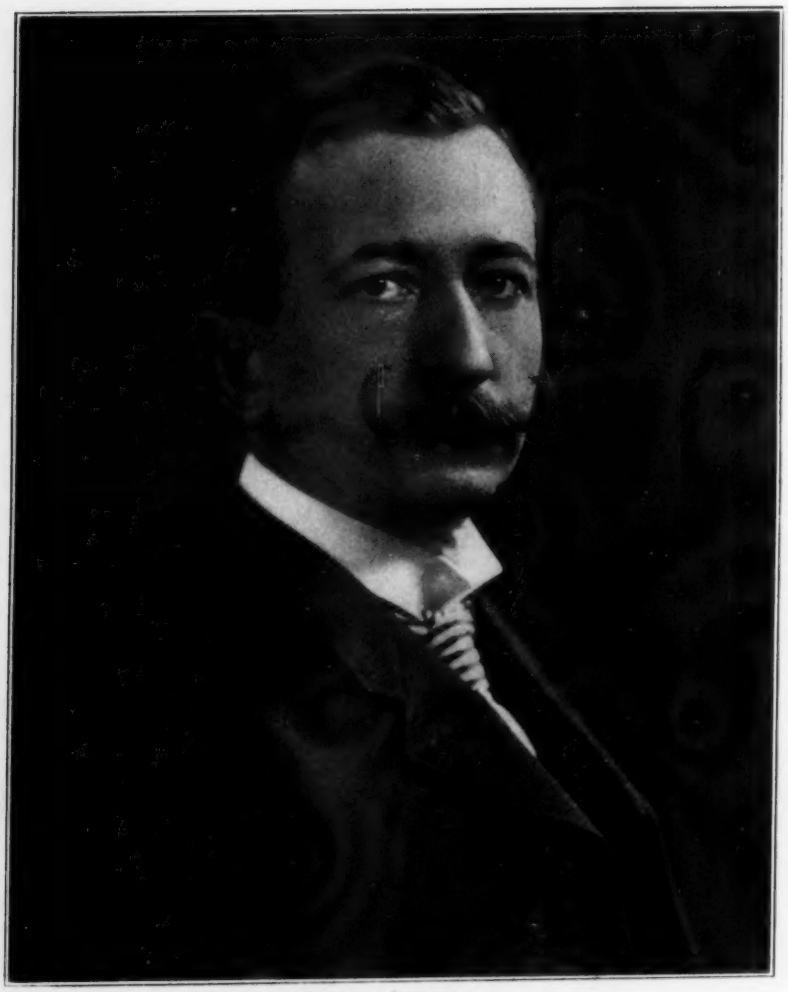

VIRGIL COBLENTZ.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXI MAY, 1932 No. 5

VIRGIL COBLENTZ.

Virgil Coblentz was born and raised in the drug business; his father, J. P. Coblentz, of Pennsylvania German extraction, was born in Hagerstown, Md.; he moved to Cincinnati in the 40's and served an apprenticeship as apothecary. He had five sons, all of whom were brought up as druggists; the father moved to Springfield, Ohio, where he opened a pharmacy in 1862 and this was operated continuously by one brother after another until 1929.

The subject of this brief sketch was born in Springfield in 1862. After graduating from Wittenberg College Academy in 1878, he was engaged in his father's pharmacy for several years and then entered Philadelphia College of Pharmacy, graduating in 1882 and winning the Procter Prize, Alumni medals with Chemistry and Materia Medica prizes. He joined the AMERICAN PHARMACEUTICAL ASSOCIATION in the year of his graduation and has now reached the fiftieth anniversary of both of these events.

After the death of his father Virgil returned to Springfield to take charge of the Coblentz Pharmacy. He was elected to membership in the Ohio State Pharmaceutical Association, and honored with the presidency in 1884 and, in the same year, successor to Professor Judge as professor of Materia Medica and Toxicology at the Cincinnati College of Pharmacy.

In the summer of 1887, Professor Coblentz left for Germany where he studied the natural sciences in the Universities of Goettingen, Strassburg and Berlin, where he earned the degree of Doctor of Philosophy.

In 1891 he returned to the United States and was elected by the Board of Trustees of the New York College of Pharmacy as professor of Pharmacy to succeed Prof. P. W. Bedford. In 1902 he was named director of the Pharmaceutical Laboratory.

During later years Dr. Coblentz spent several summer semesters studying bacteriology and pathology in Wuerzburg and Munich. In 1896 he succeeded Professor Elliott in the chair of Chemistry of the New York College which was merged as Department of Pharmacy in Columbia University.

In 1911, Dr. Coblentz resigned his professorship and laboratory connection to accept the position of chief chemist to E. R. Squibb & Sons, where he remained until 1917. He was elected *Professor Emeritus* of Chemistry of Columbia University and is now engaged in laboratory work, chiefly in analytical and research chemistry and also in pathological, bacteriological and clinical examinations.

Dr. Coblentz was *secretary* of the Scientific Section of the A. PH. A., 1896 to 1897, and its *chairman* in 1907 and 1908. He won the Ebert Prize in 1898 for his paper on "Gelsemic Acid," published in the PROCEEDINGS for 1897, pages 225 to 231. In this work he undertook the task of determining its ultimate composition.

Dr. Coblentz was associated with Dr. Charles Rice on the 7th Revision of the United States Pharmacopœia and he also served as *sub-chairman* of the Committee on Inorganic Reagents and Volumetric Solutions in the 8th and the 9th Revisions of the Pharmacopœia. He was joint author of "Sadtler & Coblentz Medical and Pharmaceutical Chemistry;" author of "Handbook of Pharmacy," five editions of "Newer Remedies" and three editons of "Volumetric Analysis." Many of his contributions to chemistry and pharmacy were published in the PROCEEDINGS of the A. PH. A. and *Journal of the Society of Chemical Industry*, *Zeitschrift fuer angewandte chemie* and *American Journal of Pharmacy*.

For a time Dr. Coblentz was contributor to "Thorpe's Dictionary of Applied Chemistry." He is a former chairman of the New York Section of the British Society of Chemical Industry and for a time chairman of the American Section of the Verein Deutscher Chemiker of Leipzig. He is *Emeritus Professor of Chemistry* of the College of Pharmacy of the City of New York.

Professor Coblentz was married in Strassburg, Alsace, in 1889. The family is graced by two sons.

FRENCH SOCIETY FOR THE HISTORY OF PHARMACY.

La Société d'Historie de la Pharmacie held its chief meeting of the year on Sunday, March 6, 1932, at the Faculté de Pharmacie de Paris, social residence of the Society, under the presidency of M. le Doyen honoraire Radais, and in the presence of M. le Doyen Guerin.

The present committee is composed of Messrs. Radais, *president*, L. G. Toraude and M. Bouvet, *vice-presidents;* Dr. Dorveaux, *permanent secretary*, E. H. Guitard, *general secretary*, and A. Royer, *treasurer*.

An account of the financial situation was given by Mr. Royer. Then Mr. Guitard's plans for various publications to be issued by the Society received the approval of the meeting, concerning the creation of a supplementary review, to be published monthly, and to be called *Dionysos*. This will be a supplement for the literary and industrial chemist; in it the names of the contributors of the society will be published. In spite of these improvements, the general meeting decided, after discussion, to hold the subscription price to 15 frs. for France and 30 frs. for foreign countries.[1]

Communications of Messrs. Bondois, Dagen and Dr. Weitz were heard; Messrs. Beytout and Guitard are named to represent the Society at the Congress of the History of Medical Sciences, to be held at Bucarest in September of this year.

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[1] Subscriptions are received at the Faculté de Pharmacie 4, avenue de l'Observatoire, Paris 6e.

EDITORIAL

E. G. EBERLE, EDITOR 10 West Chase Street, BALTIMORE, MD.

CONGRESSIONAL ACTION ON THE HEADQUARTERS BUILDING.

THE erection of the Headquarters Building has been delayed for the completion of the Government's plans for the improvement of the area in which the site is located. On May ninth, Congress approved, by resolution, the use of the property owned by the Association and such additional park property adjoining it as may be necessary to give the Building the location and setting required by these plans. This action by Congress now opens the way for building operations in the near future and provides a most ideal location for Pharmacy's Building. A long step forward has been taken toward the completion of this great undertaking of American Pharmacy.—E. F. K.

THE ST. LOUIS SURVEY.

A MOST extraordinary and unique meeting of representatives of the National Drug Industry was held in St. Louis, April 26 and 27, 1932.

These representatives were called to St. Louis to hear and study the findings and data assembled by the National Drug Store Survey, conducted by the United States Department of Commerce, coöperating with the Executive Committee of the National Drug Store Survey Committee, composed of representatives of the various drug interests of the country.

The meeting was extraordinary for many reasons, the outstanding of which was the very large attendance, numbering over 700 men, coming from thirty-two of the forty-eight states of the Union, representing the entire scope of the drug industry, ranging from the boards of pharmacy and schools of pharmacy to manufacturers, importers, wholesalers and retailers. It was a striking fact that the men representing these various interests were the high executives of the companies and associations that they represented. It was again remarkable for the intense interest and earnestness on the part of those present in the matters under consideration and their close and continued attention to the reports and discussions, and the evidence on all sides of a sincere and determined effort to set up a practical way of applying the information developed by the Survey in a form that will give the greatest benefit to the retail druggists of the country.

The work done by the Department of Commerce, coöperating with the Executive Committee, was tremendous. Never before has so searching an analysis in such great detail been made of any branch of commerce; every department of the Drug Store, from the prescription laboratory to the soda-fountain, passed under the microscopic eyes of trained research investigators; twelve months were devoted to the survey, and every type of retail drug store was studied in the investigations, this being made possible by the wonderful coöperation of the retail druggists of St. Louis. The loyal pharmacists who submitted their stores to the investigators made a real contribution in this effort to benefit their fellow pharmacists—all honor and appreciation to them.

Two days of concentrated attention to the reports culminated in a recommendation made by the "Committee on Use" of a plan to make it possible for the

retail druggists of the country to use and apply the findings of the Survey to their own stores for its benefit. The plans of the "Committee on Use" were unanimously approved at the final meeting, and these in turn, were approved by the Druggists' Research Bureau.

The recommendations of the "Committee on Use" are as follows:

"We recommend that the Druggists' Research Bureau be asked to formulate and put into execution an application plan. It is, of course, to be understood that such aid as the Bureau needs will be rendered by the National Drug Store Survey Committee through its "Committee on Use" or otherwise.

It is suggested that it might be well to consider enlarging the Bureau and perhaps also changing its name to a name in keeping with the nature of the application work.

"It is the opinion of your Executive Committee that the features listed below are important to the success of such a plan.

"1. That the work of application be under the direction of a competent individual employed full time.

"2. That ample funds be provided by contributions from manufacturers, wholesalers and retailers, and others, so that the whole industry will have an active interest in the work.

"3. That, as rapidly as practicable, demonstration stores using Survey results, be provided in sufficient numbers; suitable stores now in operation to be used for this purpose.

"4. That colleges of pharmacy be enlisted in the work of applying Survey results to these stores, and encouraged to set up model stores in their own schools to be used for purposes of instruction.

"5. That State and local retail druggists' associations be informed by the Bureau as to the results obtained in the demonstration stores and aided in organizing their members for the use of operating methods that have proven successful.

"6. That the Department of Commerce and its district offices be asked to aid in this promotion as far as practicable.

"7. That the drug trade press be enlisted to give the fullest publicity to the work of the Bureau.

"8. That local commercial organization be used wherever possible.

"9. That the work of the Bureau be presented to all meetings of drug organizations and to Drug Press.

"10. That salesmen contacting the drug trade be enlisted to give full support to the plans and distribute information.

"Your committee does not consider it advisable to attempt to offer in this report the details of an application plan; it commends for consideration, however, the plan drawn up by Mr. Robert W. Rodman and Dr. Schicks."

The Druggists' Research Bureau, after giving these recommendations consideration, reported through its chairman that the Bureau was in accord with the plans outlined by the "Committee on Use" and would coöperate with the Committee for the purpose of enlarging the scope and membership of the Bureau and, if advisable, to change the name of the Bureau, and would undertake to lay out the plans as outlined in the report of the "Committee on Use." The Bureau further recommended that, in their opinion, to carry out these plans there should be raised a fund of not less than $25,000.

"The Committee on Use" and the Bureau will confer in the near future for the purpose of setting up a satisfactory and capable organization to carry on. In the meantime, the Department of Commerce will make it possible for all interested parties to secure copies of the final reports of the Survey, when issued. Three of these final reports are now ready for such distribution, and others will soon be made available.

More and more do we hear from every quarter that has studied the machinery of distribution that the independent individual retail drug store is of major importance in this service, and the very life of the drug industry, as a whole, is dependent upon these independents taking full advantage of all available information to keep themselves profitably in business. An obligation of the independent pharmacist is to study and use every means available to him for maintaining his business on a self-respecting, dignified, profitable basis and that obligation is the great part he plays in the public health—in the health of his native land. Will he fulfil this obligation? I believe he will.—R. E. LEE WILLIAMSON.

COMMON INTERESTS.

THERE was never a time in the history of American business and the professions when a clear understanding of actual conditions and a thorough knowledge of the best methods for shaping them were more necessary than now, which signifies the importance of making full use of the meetings of national and state associations.

A very important Conference was held during the past month in St. Louis and a report on the Survey as it applies to pharmacy will be found in the addresses by Frank A. Delgado in the April number of the JOURNAL and in this issue, and also in an editorial comment of these columns. The importance of pharmacy is coming into greater evidence and a study of side-lines reveals that a profitable consideration of them may bring about a change in their complex.

The Department of Commerce is helpful to business as well as the professions and this has been shown in recent surveys wherein it has been a real assistance to business. In the St. Louis Drug Survey the opportunities for serving the profession of pharmacy have been brought forward; as a result, if the investigations are applied with a purpose to improve certain phases we may expect mutations in the drug stores and a stimulus of leading thoughts in the development of pharmacies.

There are transmutations which many would welcome, but it is to the credit of those engaged in the drug business that the service of pharmacy has been held on a high plane, so that under very difficult situations, the Government has delegated great responsibilities to the druggists, and records show that the duties and trusts assigned have been carefully and honorably discharged and guarded. There have been mistakes, but on the whole the departments of the Government have endeavored to carry on their duties with a coöperative purpose.

Taking into consideration that the activities comprising the divisions of the drug business and the profession of pharmacy have, according to the U. S. Census, contributed largely to commerce and public health and are important factors in the development of the industries, it is to us somewhat surprising that the *Nation's Business* should comment rather adversely on the National Drug Survey Conference. It seems to us the publication has tried to belittle the efforts of those who are seeking to better existing conditions and improve the service rendered by them. Everyone has a right to express opinions and to differ from others, but in our opinion, at all times, and especially in times like the present, a better Spirit of cooperation should obtain than implied by the editorial comment to which we have just referred.

The Survey undertaken by the Department, in our opinion, is not dictatorial; it may be leading, but it is informative; the thing to do is for pharmacists to study the aims and purposes of the Survey and act wisely.—Discussions are necessary, careful study and wise action are essential.

THE HALL OF SCIENCE AT A CENTURY OF PROGRESS—WORLD'S FAIR, 1933, CHICAGO.

WE ARE indebted to H. C. Christensen, *Chairman* of the Pharmacy Committee for the photograph of the Hall of Science (see "Editorial Notes"), the exterior of which is now completed. Pharmacy has been given a splendid location and accorded as much space as that allotted to the American Medical Association and the American Dental Association for their exhibits. Outside of these general display zones, there will be competitive displays by manufacturers and others. Adequate provisions have been made for the displays of exhibitors whose products are used in the medical sciences; taken as a whole the exhibits will visualize, simply yet dramatically, the tremendous strides made during the past century in the causes, detection, treatment and prevention of human and animal diseases, and planned so as to be interesting and educational to those engaged in the medical and pharmaceutical activities and to the laymen. It will develop an acquaintance with pharmacy, never before attempted and, therefore, should enlist the active interest of all pharmacists and those engaged in the related industries.

The exhibits have been classed in three general groups: Historical exhibits, illustrating the great discoveries and achievements which have revolutionized these sciences during the past century. Collective educational exhibits, depicting the present development and exhibits which will have an appeal because of their spectacular character. These groups will be more or less coördinated to illustrate the service and importance. There will be no "hands off" signs, so that the visitors may study the exhibits understandingly and derive a knowledge of the public health services, and this building is expected to become a center to which millions of people will come to absorb a new point of view and witness the miraculous changes which have occurred in the past hundred years.

"The Hall of Science, a great U-shaped building surrounding a court, will span Leif Eriksen drive at 16th Street and face the lagoon between Northly Island and the mainland. The building will rise from colored terraces, two stories and a mezzanine in height and will be 700 feet long and 400 feet wide. In its court will be a huge rostrum with bas-relief ornaments. At one corner of the building will rise a 176-foot tower filled with a carillon. The Hall of Science will be brightly colored and brilliantly illuminated at night." It is the purpose from time to time to have descriptive articles in the JOURNAL, so that information may be gained by the readers of pharmacy's part in this wonderful exhibit.

SCIENTIFIC SECTION

THE CHEMICAL AND BIOLOGICAL STANDARDIZATION OF OLEORESIN OF ASPIDIUM.*

BY M. L. PABST AND A. RICHARD BLISS, JR.[1]

In 1830 Aspidium Filix-mas was introduced in both editions (Philadelphia and New York) of the U. S. Pharmacopœia, but was included in the Secondary List only. In 1860 it was transferred to the Primary List, and in 1880 it became official under its present title "Aspidium" (10). The crude drug itself has been employed very rarely in medicine since the introduction of the Oleoresin.

The constituents which are present in the crude drug are also presumably present in the Oleoresin (17). Although the literature shows little disagreement as to the constituents which are present in Aspidium, there is some debate as to which of these are the active anthelmintic agents.

Sollmann (18) states that the active constituents of Aspidium are *amorphous filicic acid* ($C_{33}H_{40}O_{13}$), *aspidinin*, *albaspidin*, *flavaspidic acid*, *aspidin*. He states further that the *amorphous filmaron* ($C_{47}H_{54}O_{13}$) is perhaps an impure filicic acid; and that the inactive constituents are crystalline *filicic acid* or *filicin* ($C_{35}H_{38}O_{11}$), and *aspidinol*. He suggests that the crystalline filicic acid is the lactone of the active amorphous acid, the two being readily converted into each other. Solis-Cohen (17) adds *filic acid* ($C_{35}H_{38}O_{12}$), filix-tannic acid, a green fixed oil, volatile oil, sugar, starch, resin and wax to the foregoing list. Amorphous filicic acid or filicin has been credited as the important anthelmintic constituent of Male Fern. However, this does not exclude the other constituents as possible anthelmintic agents or synergists, for some of them, at any rate are toxic (14). Shoemaker (16), quoting Kobert, makes the definite statement that the anthelmintic action of the Oleoresin of Aspidium does not depend solely on the filicic acid present, but also on the ethereal oils; while Kraft, according to Thorpe (21), believes that the anthelmintic action of the drug is due primarily to filmaron ($C_{47}H_{54}O_{16}$), an amorphous, brownish yellow acid which melts at 60° C., and marketed (7) as a 10% solution in Castor Oil called "Filmaron Oil."

Several different chemical formulas have been assigned to amorphous filicic acid. Solis-Cohen (17) gives the formula $C_8H_{10}O_5$; Thorpe (21), $C_{35}H_{42}O_{13}$ or $C_{35}H_{40}O_{13}$ for the active form, and quotes Poulsson's formula $C_{35}H_{40}O_{12}$, and Boehm's $C_{35}H_{38}O_{12}$ for the inactive. Sollmann (18) and Poulsson (13) agree with the formula $C_{35}H_{40}O_{13}$. Evers (5) concurs in both formulas for the active form as given by Thorpe. Fuller (7) quotes the following formulas: Luck, $C_{26}H_{30}O_9$; Grabowski, $C_{14}H_{18}O_5$; Gallas, $C_{18}H_{22}O_6$; and Daccoma, $C_{14}H_{16}O_5$. Hare (9) accepts the last formula. Green (8) places Aspidium and its constituents in the Phloroglucinol-Butyric Acid group or the Phloroglucinol group, because he found phloroglucinol and butyric acid among the decomposition products following acid or alkaline hydrolysis of an Aspidium extract. He points out by structural formulas the relationship between phloroglucinol and the constituents of Aspidium. On examin-

* Scientific Section, A. PH. A., Miami meeting, 1931.

[1] Laboratories of Pharmacology, University of Tennessee (Memphis).

ing these structural formulas it appears that aspidinol and filicic acid may be cleavage products of aspidin. The carbon bridge in his formula for filmaron is accepted as the reason for its instability. Green suggests the decomposition of filmaron during the manufacture of the Oleoresin as the possible reason for the presence of some of the other constituents of this drug.

THE STANDARDIZATION OF ASPIDIUM.

Until the appearance of the Tenth Revision of the U. S. Pharmacopœia (12) there was no official requirement as to the percentage of crude filicin present in the Oleoresin of Aspidium. Oleoresins were marketed which contained varying percentages of filicin. Berg (1) reported samples varying from 8 to 26 per cent of filicin. The report of the Committee on Drug Market of the AMERICAN PHARMACEUTICAL ASSOCIATION (22) in 1918 included samples which assayed only 8 per cent of crude filicin. Linke (26) found some 1-Gm. capsules which assayed from 5.45 to 14.22 per cent of crude filicin, and some commercial oleoresins which contained from 19 to 27 per cent.

The need for a carefully standardized product was generally recognized (3), especially in view of the fact that, when used in therapeutics, as large a dose is administered as the physician dares to employ, and the patient is possibly bordering on poisoning. The fact that a physiologically inactive drug cou'd meet the microscopic requirements given in the Ninth Revision of the U. S. Pharmacopœia was further evidence that an assay was needed (4). Accordingly, the Tenth Revision of the U. S. Pharmacopœia requires not less than 24 per cent of crude filicin to be present in the Oleoresin, and presents a chemical method for the determination of the filicin.

The consensus of opinion seems to be that chemical methods for the assay of Aspidium and of Oleoresin of Aspidium do not provide very satisfactory indices of the therapeutic worth of these agents (23). For purposes of standardization by chemical methods the active constituents of Aspidium has been assumed to be crude filicic acid. However, this is actually a mixture of complex composition, and no reliable methods have been devised to date by which each of the constituents may be accurately determined. A further claim is that crude filicic acid is accompanied by inert constituents in varying and unknown amounts.

Chemical assay methods usually involve, in the case of the crude drug, (*a*) the determination of the oleoresin, and (*b*) the determination of the crude filicic acid in the oleoresin thus obtained. In the case of the Oleoresin of Aspidium "(*b*)" alone is carried out. The U. S. P. X method for obtaining the oleoresin, and the U. S. P. X process for the assay of Oleoresin of Aspidium, in so far as the literature indicates, appear to be as satisfactory as any of the chemical methods which thus far have been proposed for the evaluation of this drug. However, there is one modification of the U. S. P. X assay of Oleoresin of Aspidium which will be referred to presently.

Many are of the opinion that biological methods for the evaluation of Aspidium and its Oleoresin give more trustworthy pictures of the therapeutic possibilities of these agents.

The Sub-committee on Biological Assays of the U. S. P. (XI) Revision Committee appointed a special Group Committee on Aspidium Assay. In an effort to obtain some working data which might be submitted to the members of this group

committee for collaborative study, this comparative study of the standardizing methods thus far used was carried out by the authors, with these objects in view: (*a*) possible improvements in the present official chemical assay procedure; (*b*) a more satisfactory, practical and simple biological assay; and (*c*) the relation, if any, which may exist between the percentage of filicin present in Oleoresin of Aspidium and the biological potency.

1. CHEMICAL METHODS.

Various chemical assays have been used for the quantitative determination of crude "filicin" in the Oleoresin of Aspidium.

The U. S. Pharmacopœial Method (12) is as follows:

"Warm the oleoresin on a water bath and stir until it is thoroughly mixed. Transfer about 5 Gm., accurately weighed, to a 200-cc. flask, dissolve in 40 Gm. of ether, and add 100 Gm. of an aqueous solution of barium hydroxide (3 to 100), and shake vigorously for 5 minutes. Allow the liquids to separate and filter off 86 Gm. of the aqueous fluid. Transfer this to a separator, add sufficient hydrochloric acid to produce a distinctly acid reaction, and extract with three successive portions of 30 cc., 20 cc. and 15 cc. of ether. Draw off and combine the ethereal solutions, filter, wash the filter with ether, evaporate, and dry the residue to a constant weight at 100° C. This residue weighs not less than 0.96 Gm., corresponding to not less than 24 per cent of crude filicin."

In the foregoing assay it is presumed that there are 1.25 Gm. of crude filicin in 5 Gm. of the Oleoresin, which is equivalent to a 25 per cent yield. Also, the aliquot portion, 86 Gm., is supposedly equivalent to 4 Gm. of Oleoresin, and contains 0.96 Gm. of crude filicin, which represents a 24 per cent yield. The aqueous layer contains *about* 6.25 Gm. of ether. Evidently, the aqueous layer may contain *more or less* than that amount. Accordingly, in weighing the aliquot portion there may be more or less than the equivalent of 4 Gm. of the Oleoresin, and consequently this element in the method Mr. Pabst suggests may lead to varying results.

The British Pharmacopœia Method (2) is almost identical with the U. S. P. method with only two minor differences. Instead of dissolving the 5 Gm. of Oleoresin in 40 Gm. of ether, 40 cc. of ether are used. In determining the percentage of crude filicin the statement appears that the residue should weigh not less than 0.8 Gm., which is equivalent to 20 per cent.

The Swiss Pharmacopœial Method (20) is carried out in the same manner as the two preceding methods with but two minor changes. The 5 Gm. of Oleoresin are dissolved in 30 Gm. of ether instead of 40 Gm., as directed in the U. S. Pharmacopœia, and 40 cc. in the British Pharmacopœia. The residue should weigh 1.04 to 1.12 Gm., corresponding to 26 to 28 per cent of crude filicin.

Fluck (6) recommends a slight change in the Swiss method. Instead of drying the residue to constant weight, he suggests drying for one hour only at 100° C. However, drying the residue for one hour only apparently fails to drive off all of the moisture, because continued heating causes the residue to lose, if so dried, considerable more weight. The results by this method are, of course, higher.

Lyons (11) suggests a modification of the Swiss method as follows:

"Dissolve 5 Gm. of the Oleoresin, accurately weighed, in 40 cc. of ether. Add 100 cc. of a 3% solution of barium hydroxide and shake vigorously for 5 minutes. Transfer to a separator, allow to stand for 10 minutes, filter and draw off 87 cc. To this add sufficient hydrochloric

acid to render it distinctly acid and shake out the precipitated filicic acid with three successive portions of 30 cc., 20 cc. and 15 cc. of ether. Filter the ether through cotton, evaporate and dry the residue to constant weight at 100° C."

Each of the foregoing methods is an aliquot portion method, and, if the objection suggested in the case of the U. S. P. method holds, then the same objection applies equally to each of the modified methods and related methods above.

2. BIOLOGICAL METHODS.

Sollmann's Earthworm Method (19) is as follows:

"The Oleoresin is shaken, and a very small drop (approximately 0.1 cc.) is placed on a small tared filter paper, weighed, and rubbed thoroughly with sand in a mortar, adding the BB solution (bilein, 0.04%; sodium bicarbonate, 1%; probably a 1% solution of sodium bicarbonate could be used as some comparative experiments show no essential difference), using 50 cc. of the solution for 0.01 Gm. of the Oleoresin. This is filtered, and represents 2 mg. of the Oleoresin per 10 cc. of the stock solution.

"The dilutions are made up in urine glasses as follows:

0.01 Gm. per 100 cc.—equals 50 cc. of the stock solution and water q. s. ad 100 cc.
0.005 Gm. per 100 cc.—equals 25 cc. of the stock solution and water q. s. ad 100 cc.
0.003 Gm. per 100 cc.—equals 15 cc. of the stock solution and water q. s. ad 100 cc.
0.002 Gm. per 100 cc.—equals 10 cc. of the stock solution and water q. s. ad 100 cc.
0.001 Gm. per 100 cc.—equals 5 cc. of the stock solution and water q. s. ad 100 cc.

"Five worms are placed in each glass and observed after 24 hours. A standard Oleoresin should kill the worms in 0.002 to 0.003%, differing probably a little with the season. Until this point is determined, it may be advisable to check the preparation to be tested against a preparation of known strength (*i. e.*, one that is fatal with 0.003%, and only depressant with 0.002% in cold weather)."

The major criticism of the Sollmann Earthworm Method is the length of time involved.

Zoltan's Method (25) is as follows:

"The ethereal extract of Male Fern is carefully warmed to 40° C. and well stirred. Four grams (4 Gm.) of the extract are then emulsified with powdered acacia and a 1% solution of sodium bicarbonate. This emulsion is diluted to 2000 cc. with tap water containing 1% of sodium bicarbonate; 500 cc. of the latter, equal to 1 Gm. of the extract, are again diluted with sodium bicarbonate solution to 2000 cc. This standard solution, containing 0.1 Gm. of the extract in 200 cc., can be used after 2 hours. The minimal lethal dose is fixed in several stages. A number of solutions are prepared, varying considerably in concentration; then two extreme values must be found, where either all of the animals are killed within 2 hours, or where they remain alive. At least six leeches, weighing between 3 and 5 Gm. must be used. In the second stage these two values must be brought so close that with the higher value the leeches just perish within two hours, while the lower value does not kill them. A third stage is employed to establish a biological average value, where about half the number of leeches are destroyed within two hours, the other half after the lapse of two hours. This value represents the minimal lethal dose. In 100 cc. of the standard extract, as above, the higher value was found to be 0.0036, the lower 0.002."

As far as the time element and the dilutions are concerned, this method appears to be satisfactory. However, leeches are difficult to keep as reserve specimens, and, added to this, is the difficulty in obtaining them.

Wasicky and Becker (24) recommend a biological assay in which fish are exposed to varying concentrations of the preparations. In a large number of experiments,

however, they found no parallel between the amounts of filicin obtained by chemical methods and the results by their biological procedure.

Schamelhout (15) recommends a biological assay with earthworms or small fish as the standardizing agent. The dilution of 0.002 parts to 100 parts is stated as the minimum concentration which will produce death. No time factor is introduced, however. Experimental work of this type with gold fish in the laboratories of the Division of Pharmacology of the University of Tennessee has shown that these animals do not react uniformly to drugs, and are not particularly adaptable to biological assay methods.

3. THE MATERIALS USED.

Two samples of powdered Aspidium and six samples of Oleoresin of Aspidium were purchased on the open market. Microscopic examinations (A. John Schwarz) demonstrated that the crude drugs were Aspidium Filix-mas with no adulterations. Chemical and physical examinations showed the absence of adulterants in the samples of Oleoresin.

Oleoresins were preparated from each of the powders, the method of the U. S. P. X being used.

One of the powders yielded but 0.7% of Oleoresin, and this was not used in any of the additional experimental work because the material was too limited. The second powder yielded 9.44% of Oleoresin.

The Oleoresins purchased were all of a dark green color, thick and with the characteristic odor and other common properties required in the official specifications. The specific gravities varied from 1.001 to 1.017.

4. SUGGESTED CHANGE IN U. S. P. X METHOD.

The following modified method was devised during the course of the study, and the results obtained apparently justify its proposal as a more reliable and more accurate chemical method.

The Procedure: Warm the Oleoresin on a water-bath and stir until it is thoroughly mixed. Transfer about 3 Gm., accurately weighed, to a 250-cc. flask, dissolve in 40 cc. of ether, add 75 cc. of a 3% aqueous solution of barium hydroxide and shake vigorously for 5 minutes. Transfer this mixture to a separator. Allow the liquids to completely separate, draw off and filter the barium hydroxide layer. Rinse the 250-cc. flask with two 25-cc. portions of a 3% aqueous barium hydroxide solution. After each rinsing, transfer the barium hydroxide solution to a separator, shake for one minute, allow the liquids to separate completely, draw off and filter the barium hydroxide layer. Transfer the combined filtered barium hydroxide solutions to a separator, make distinctly acid (to litmus) with concentrated hydrochloric acid and extract with three successive portions of 30 cc., 20 cc. and 15 cc. of ether. Draw off the combined ethereal solutions, filter, wash the filter with ether, evaporate and dry the residue to constant weight at 100° C.

The procedure was checked by blank tests. This modified method presents several possible advantages. The chances of error are apparently reduced, in view of the statements above, since an aliquot portion is not used, but instead the entire aqueous fraction. Less time is required in carrying out this method, since it is not necessary to determine the specific gravity, or to weigh the barium hydroxide, the ether and the portion of the aqueous layer. By using a smaller amount of Oleo-

resin, the residue is less, and, consequently, may be dried to constant weight more rapidly.

The method presents one possible disadvantage in the hands of the inexperienced worker. Occasionally, with some Oleoresins, an emulsion is formed which is quite stable. If the worker is careful, this may, however, be avoided.

5. COMPARATIVE RESULTS OBTAINED BY THE CHEMICAL METHODS.

The U. S. P. X Method, representative of the group discussed above, and the suggested modified method were employed in this portion of the comparative study. Three assays were carried out on each Oleoresin by each method. The results are tabulated below.

TABLE I.—CHEMICAL ASSAY OF OLEORESIN OF ASPIDIUM.

Method and Sample.	Per Cent of Filicin. Assay 1.	Assay 2.	Assay 3.	Average.	Variation.
Modified; Sample B	3.03	2.95	2.98	2.98	0.08
U. S. P. X; Sample B	3.12	2.94	2.85	3.00	0.27
Modified; Sample C	24.53	24.50	24.58	24.53	0.08
U. S. P. X; Sample C	25.60	25.32	25.51	25.47	0.28
Modified; Sample D	25.05	25.00	25.02	25.02	0.05
U. S. P. X; Sample D	26.20	25.87	26.01	26.02	0.33
Modified; Sample E	20.13	18.42	18.82	19.15	0.71
U. S. P. X; Sample E	20.50	21.02	20.41	20.64	0.61
Modified; Sample F	23.66	23.61	23.68	23.65	0.07
U. S. P. X; Sample F	24.90	25.13	25.02	25.01	0.23
Modified; Sample G	24.80	24.83	24.87	24.83	0.07
U. S. P. X; Sample G	26.01	26.24	25.82	26.01	0.42
Modified; Sample H	24.53	24.51	24.57	24.40	0.06
U. S. P. X; Sample H	23.82	24.35	24.11	24.09	0.53

The results tabulated above show that there is a greater variation in the percentages obtained by the U. S. P. X Method than by the Modified Method. Loss of ether by vaporization may explain in part the greater variation and the higher yield.

6. RESULTS OBTAINED BY A BIOLOGICAL METHOD, AND A COMPARISON WITH THE CHEMICAL METHOD.

A combination of the Sollmann and the Zoltan methods, somewhat modified by the workers, was studied, with the added object of determining whether or not any parallelism could be demonstrated. The thought presented itself that, since Ascarides obtained from hogs represented more closely the type of worms found in the intestinal tracts of the human and of the dog, this type of worm might lend itself more satisfactorily to a biological assay of this anthelmintic drug. Accordingly, supplies of this worm were obtained from the slaughter-house and used in this study.

A stock solution was made according to Zoltan's method, the dilution used representing 0.1 Gm. of the Oleoresin in 200 cc. of the emulsion (50 mg. per 100 cc.). Sollmann's method of diluting the foregoing stock solution was employed, a 1% solution of sodium bicarbonate being used, however, instead of tap water, in making up the dilutions. The dilutions used ranged from 1 mg. per 100 cc. to 10 mg. per 100 cc. (1, 2, 3, 5 and 10). Fresh supplies of worms, removed directly from the

intestine of the hog, were employed. Observations were made over a period of 48 hours with 42 series of worms. The records show that the worms in all cases but one lived through the end of the observation period. Death occurred in but one dilution, *viz.*, 1 mg. per 100 cc., and in this dilution the worms were alive for a period of 14 hours or more. Check worms, kept in physiological saline solution, remained normal over a period of four or five days. Similar checks and results were obtained with 1% sodium bicarbonate solution. The results showed that Ascarides are not uniformly susceptible to the Oleoresin. In view of these findings it is obvious that this type of worm does not lend itself to biological assays of Aspidium.

The experiments were then repeated using earthworms, which Sollmann states resemble intestinal worms in their reactions toward some anthelmintics. These worms are readily obtained and are easily kept. Preliminary experiments were carried out to determine what dilution might prove most satisfactory with this worm. Series were run with dilutions containing 1 mg., 2 mg., 3 mg., 5 mg., 10 mg. and 50 mg. per 100 cc. With three, *viz.*, the 5-, 10- and 50-mg. dilutions, the worms were killed within 12 hours, the other dilutions requiring a much longer time. The 50-mg. dilution killed the worms in 3 hours; the 10 mg., in 10 hours; and the 5 mg. in 12 hours. The 2-mg. dilution required 24 hours for death; and with the 1 mg. the worms were still alive at the end of 24 hours. Consequently, because of the convenient time factor, it was decided to use the 50-mg. dilution with six samples of the Oleoresin already studied chemically. The observations are recorded in the tables which follow.

TABLE II.—BIOLOGICAL ASSAY OF OLEORESIN B.

Dilution mg. per 100 cc.	Time in Hours after Placing Ascarides in Dilutions: 10.	12.	14.	24.	26.	28.	30.	32.	34.	36.	38.
1 mg.	A*	A	A	A	A	A	A	A	I*	I	I
2 mg.	A	A	A	A	A	A	A	A	A	A	A
3 mg.	A	A	A	A	A	A	A	A	A	A	A
5 mg.	A	A	A	A	A	A	A	A	A	A	A
10 mg.	A	A	A	A	A	A	A	A	A	A	A
50 mg.	A	A	A	A	A	A	A	A	A	A	A

* Indicates: "A"—alive; "I"—paralyzed or dead.

In this series all the worms were alive up to a period of 34 hours. All were alive at the end of the experiments except in one concentration; *viz.*, the dilution of 1 mg. per 100 cc. at 34 hours.

TABLE III.—BIOLOGICAL ASSAY OF OLEORESIN C.

Dilution mg. per 100 cc.	Time in Hours after Placing Ascarides in Dilutions. 10.	12.	14.	24.	26.	28.	30.	32.	34.	36.	48.
1 mg.	A	A	A	A	A	A	A	A	A	A	A
2 mg.	A	A	A	A	A	A	A	A	I	I	I
3 mg.	A	A	A	A	A	A	A	A	A	A	A
5 mg.	A	A	A	A	A	A	A	A	A	A	A
10 mg.	A	A	A	A	A	A	A	A	A	A	A
50 mg.	A	A	A	A	A	A	A	A	A	A	A

All of the worms treated with Oleoresin C were alive over a period of 34 hours. In only one case the worms died. In the dilution of 2 mg. per 100 cc. they were alive up to 34 hours.

TABLE IV.—BIOLOGICAL ASSAY OF OLEORESIN E.

Dilution mg. per 100 cc.	Time in Hours after Placing Ascarides in Dilutions: 10.	12.	14.	24.	26.	28.	30.	32.	34.	36.	48.
1 mg.	A	A	A	I	I	I	I	I	I	I	I
2 mg.	A	A	A	I	I	I	I	I	I	I	I
3 mg.	A	A	A	I	I	I	I	I	I	I	I
5 mg.	A	A	A	A	A	I	I	I	I	I	I
10 mg.	A	A	A	A	A	A	A	A	A	A	A
50 mg.	A	A	A	A	A	A	A	A	A	A	A

The results in the above series show that death occurred in 24 hours in the dilutions of 1 mg. per 100 cc., 2 mg. per 100 cc. and 3 mg. per 100 cc.; and in 28 hours in 5 mg. per 100 cc. In the other two dilutions, 10 mg. per 100 cc. and 50 mg. per 100 cc. the worms were still alive at the end of the observations.

TABLE V.—BIOLOGICAL ASSAY OF OLEORESIN F.

Dilution mg. per 100 cc.	Time in Hours after Placing Ascarides in Dilutions: 10.	12.	14.	24.	26.	28.	30.	32.	34.	36.	48.
1 mg.	A	A	A	A	A	A	I	I	I	I	I
2 mg.	A	A	A	I	I	I	I	I	I	I	I
3 mg.	A	A	A	A	A	A	A	A	I	I	I
5 mg.	A	A	A	A	A	A	A	A	A	A	A
10 mg.	A	A	A	A	A	A	A	A	I	I	I
50 mg.	A	A	A	A	A	A	A	A	A	A	A

Results reported in Table V show no relation between the death period and concentrations. Death occurred in the dilution of 1 mg. per 100 cc. at the 30th hour; in the 2 mg. per 100 cc. at the 24th hour; in the 3 mg. per 100 cc. and the 10 mg. per 100 cc. at the 34th hour, while in the other dilutions of 5 mg. per 100 cc., and 50 mg. per 100 cc., the worms remained alive until the end of the observations.

TABLE VI.—BIOLOGICAL ASSAY OF OLEORESIN G.

Dilution mg. per 100 cc.	Time in Hours after Placing Ascarides in Dilutions: 10.	12.	14.	24.	26.	28.	30.	32.	34.	36.	48.
1 mg.	A	A	A	A	A	A	A	A	A	A	A
2 mg.	A	A	A	A	I	I	I	I	I	I	I
3 mg.	A	A	A	A	A	A	A	I	I	I	I
5 mg.	A	A	A	A	A	I	I	I	I	I	I
10 mg.	A	A	A	A	A	A	A	A	I	I	I
50 mg.	A	A	A	A	A	A	A	A	A	A	A

Death, in this series, occurred in the dilutions of 2 mg. per 100 cc. in 26 hours; 3 mg. per 100 cc. in 32 hours; 5 mg. per 100 cc. in 28 hours; and 10 mg. per 100 cc. in 34 hours, while in the weakest, 1 mg. per 100 cc. and the strongest preparations, 50 mg. per 100 cc., the worms lived until the end of the observations.

TABLE VII.—BIOLOGICAL ASSAY OF OLEORESIN H.

Dilution mg. per 100 cc.	Time in Hours after Placing Ascarides in Dilutions: 10.	12.	14.	24.	26.	28.	30.	32.	34.	36.	48.
1 mg.	A	A	A	I	I	I	I	I	I	I	I
2 mg.	A	A	A	A	A	A	A	A	A	A	A
3 mg.	A	A	A	A	A	A	A	A	A	A	A
5 mg.	A	A	A	A	A	A	A	A	A	A	A
10 mg.	A	A	A	A	A	A	A	A	A	A	A
50 mg.	A	A	A	A	A	A	A	A	A	A	A

The results in this series show that the worms in all cases but one lived until the end of the observations. Death occurred in only one dilution, 1 mg. per 100 cc., and in this dilution the worms were alive for a period of 14 hours or more.

TABLE VIII.—BIOLOGICAL ASSAY OF OLEORESIN F.

Dilution mg. per 100 cc.	Time in Hours after Placing Earthworms in Dilutions: 1.	2.	3.	4.	6.	7.	10.	12.	14.	24.
1 mg.	A	A	A	A	A	A	A	A	A	A
2 mg.	A	A	A	A	A	A	A	A	A	A
3 mg.	A	A	A	A	A	A	A	A	A	I
5 mg.	A	A	A	A	A	A	A	I	I	I
10 mg.	A	A	A	A	A	A	I	I	I	I
50 mg.	A	A	I	I	I	I	I	I	I	I

A study of the table above shows that out of the six preparations used only three—the 5 mg. per 100 cc., the 10 mg. per 100 cc. and the 50 mg. per 100 cc.—kill the worms within 12 hours, the others requiring a much longer period of time. These, therefore, appear to be the more satisfactory dilutions to use for biological assay purposes. A short assay is preferable for several reasons; *viz.*, less time is required to complete the experiment; the experimental animal is not subjected to abnormal conditions for so long a time, thus giving more accurate results; and, if a substance is to be used on man as an anthelmintic, it must prove efficacious in a relatively short time, since retention in the intestine may prove harmful to the host. Accordingly, the dilution, 50 mg. per 100 cc., was used in the following assay method.

Emulsions containing 50 mg. of the Oleoresin in each 100 cc. were prepared from Oleoresins C, D, E, F, G and H. Ten checks were carried out on each Oleoresin. A worm was placed in each of ten 150-cc. beakers, each containing 100 cc. of the emulsion. The results of these experiments follow.

TABLE IX.—BIOLOGICAL ASSAY OF OLEORESIN C.

Time after Placing Worms in Dilutions.	Earthworm: 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1 hour	A	A	A	A	A	A	A	A	A	A
2 hours	A	A	I	I	I	I	I	I	I	I
3 hours	I	I	I	I	I	I	I	I	I	I

TABLE X.—BIOLOGICAL ASSAY OF OLEORESIN D.

Time after Placing Worms in Dilutions.	Earthworm: 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1 hour	A	A	A	A	A	A	A	A	A	A
2 hours	A	A	I	I	I	I	I	I	I	I
3 hours	I	I	I	I	I	I	I	I	I	I

TABLE XI.—BIOLOGICAL ASSAY OF OLEORESIN E.

Time after Placing Worms in Dilutions.	Earthworm: 1.	2.	3.	4.	5.	6.	7.	8	9.	10.
1 hour	A	A	A	A	A	A	A	A	A	A
2 hours	A	A	A	A	A	A	A	A	A	A
3 hours	A	A	A	A	A	A	I	I	I	I
4 hours	A	A	A	A	A	I	I	I	I	I
5 hours	A	I	I	I	I	I	I	I	I	I
6 hours	I	I	I	I	I	I	I	I	I	I

TABLE XII.—BIOLOGICAL ASSAY OF OLEORESIN F.

Time after Placing Worms in Dilutions.	Earthworm: 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1 hour	A	A	A	A	A	A	A	A	A	A
2 hours	A	I	I	I	I	I	I	I	I	I
3 hours	I	I	I	I	I	I	I	I	I	I

TABLE XIII.—BIOLOGICAL ASSAY OF OLEORESIN G.

Time after Placing Worms in Dilutions.	Earthworm: 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1 hour	A	A	A	A	A	A	A	A	A	A
2 hours	A	A	A	I	I	I	I	I	I	I
3 hours	I	I	I	I	I	I	I	I	I	I

TABLE XIV.—BIOLOGICAL ASSAY OF OLEORESIN H.

Time after Placing Worms in Dilutions.	Earthworm: 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1 hour	A	A	A	A	A	A	A	A	A	A
2 hours	A	A	A	I	I	I	I	I	I	I
3 hours	I	I	I	I	I	I	I	I	I	I

In each series with each Oleoresin the 50-mg. dilution failed to kill the earthworm in 1 hour; from 60 to 90% of the earthworms were killed by this dilution in a 2-hour period with five of the six Oleoresins, 0% being killed in the case of the sixth sample; 100% of the earthworms were killed in the cases of 5 of the 6 samples in the 3-hour period, the sixth sample showing but 40% killed. Controls were carried out as with the other experiments.

In the cases of the 5 samples which, in the 50-mg. dilutions, killed 100% of the earthworms in 3 hours, chemical assays disclosed from 23.65 to 25.02% (average, 24.48%) of crude filicin. The sixth Oleoresin assayed chemically but 19.15%, and a period of six hours was required to kill all of the earthworms.

CONCLUSIONS.

1. A study of the published chemical assay methods shows them to be more or less unsatisfactory, since they apparently determine relative rather than absolute percentages of filicin present.

2. A comparative study of the Modified Method and the U. S. P. X Method, representative of practically all of the reported chemical methods, showed that the Modified Method is more accurate, more rapid and less complicated.

3. Powdered Aspidium and Oleoresin of Aspidium which fail to meet the U. S. P. requirements are sold on the open market.

4. Oleoresins prepared from powdered Aspidium which meets the U. S. P. requirements do not always assay chemically 24% of crude filicin.

5. Ascarides cannot be used for biological assay of this drug. Earthworms are satisfactory.

6. The biological assay study with earthworms shows that the percentage of crude filicin is a definite indication of the anthelmintic powers of Oleoresin of Aspidium.

NOTE: It is planned to carry on collaborative studies of the chemical and the biological assay procedures suggested in this paper with samples of (*a*) the Oleoresin itself, (*b*) of crude filicin, and (*c*) of the residue remaining after the extraction of the crude filicin.

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ARGENTINE PHARMACEUTICAL CONGRESS.

The second Argentine Pharmaceutical Congress will be held at Buenos Aires in August. One of the items on the program will be a discussion of pharmacy laws of various countries.

A NOTE ON THE ASSAY OF HYOSCYAMUS.[1]

BY N. C. SCHALLER AND L. H. BALDINGER.[2]

The present method of the United States Pharmacopœia for the assay of hyoscyamus and its preparations has been subject to much criticism but, although the literature on the subject is extensive, no definite modifications have been suggested. The amount of alkaloid in the tincture, as well as in the crude drug, is so minute that it is difficult to obtain closely-agreeing results by the present method of analysis.

Caines (1) made a study of several methods for the assay of hyoscyamus and its extracts with the view of ascertaining whether the assay methods for belladonna were applicable to hyoscyamus. Markwell and Walker (2) noted that the method of the British Pharmacopœia for the assay of belladonna leaves is not identical with that of the extract and the tincture. In the former case no heat is used to drive off the chloroform before titration, while in the latter case the chloroformic extract is heated, thereby driving off the volatile alkaloids and causing low and inconsistent results. Exler (3), after a study of the stability of hyoscyamine under conditions experienced in assay procedures, advises the avoidance of assay procedures which will tend to hydrolyze the alkaloids. Reindollar (4) has shown that the U. S. P. X method for the assay of tincture of hyoscyamus is not sufficiently accurate to insure concordant results in the hands of different skilled analysts using special precautions as suggested by Mr. Reindollar. He prepared a specimen with great care and submitted portions to each of three expert analysts. The results were not in agreement, although each chemist checked his own results quite well. Stikarofsky (5) submitted specimens of tincture of hyoscyamus to four independent analysts to be assayed according to the U. S. P. X method. These results did not check and he concluded that the variations were due, at least in part, to prolonged heating of the alkaloidal extractions before titrating. The U. S. P. X in referring to the evaporation of solvents specifies that, due to the sensitivity of the alkaloids of hyoscyamus to heat, the solutions of these alkaloids should not be evaporated to dryness on a water-bath. It was suggested that the drug and the tincture be assayed by the U. S. P. X method with the slight modification that no heat be used in any of the evaporations.

The U. S. P. X type process B for drugs and type process D for galenicals were used, respectively, for the assay of the crude drug and the tincture. In order to hasten and facilitate evaporation of the alcohol from the tincture, and the solvent from the immiscible-solvent extractions, a vacuum desiccator was used. This was fitted with a two-hole rubber stopper through which were inserted two glass tubes, one of which was drawn out into a very fine capillary, which dipped just below the surface of the liquid undergoing evaporation. This solution can be placed in a deep crystallization dish of suitable diameter to fit into the desiccator. By applying suction to the other tube, a very fine stream of air bubbles can be drawn through the solution. By means of a screw-clamp and rubber tube attached to the glass tube drawn into a capillary the stream of air bubbles and the amount of vacuum

[1] Abstracted from a thesis presented as partial fulfilment for the degree of Bachelor of Science to the Department of Pharmacy, University of Notre Dame, by N. C. Schaller.

[2] Instructor, Department of Pharmacy, University of Notre Dame, Notre Dame, Ind.

can be regulated. The temperature of the laboratory in which the samples were analyzed varied from 18°–25° C. In the titration of the alkaloids, twentieth-normal acid was substituted for tenth-normal acid, and a dilution of methyl red, the indicator used, was kept nearby as a comparator for the end-points, all of which were run to a standard tint. In order to show the comparison between the U. S. P. X method and the same method without any heat being used in the evaporations, the crude drug and the tincture were assayed by both procedures and the results are shown in the following tables:

TABLE I.—ASSAY OF CRUDE DRUG.

Results expressed as % total alkaloids (as Hyoscyamine).

U. S. P. X Method.		U. S. P. X Method, Absence of Heat, Use of Vacuum Desiccator for Evaporation of Solvents.	
Sample 1	0.054	Sample 1	0.075
2	0.052	2	0.077
3	0.050	3	0.074
4	0.055	4	0.076
5	0.049	5	0.077
Average	0.052	Average	0.076

TABLE II.—ASSAY OF TINCTURE OF HYOSCYAMUS.

Results expressed as grams per 100 cc. of total alkaloids (as Hyoscyamine).

U. S. P. X Method.		U. S. P. X Method, Absence of Heat, Use of Vacuum Desiccator for Evaporation of Solvents.	
Sample 1	0.00514	Sample 1	0.00836
2	0.00448	2	0.00707
3	0.00321	3	0.00770
4	0.00386	4	0.00717
5	0.00257	5	0.00900
6	0.00323	6	0.00885
7	0.00295	7	0.00805
8	0.00350	8	0.00779
9	0.00250	9	0.00811
10	0.00523	10	0.00830
Average	0.00367	Average	0.00804

SUMMARY.

The U. S. P. X method for the assay of the tincture of hyoscyamus, as well as for the crude drug, appears to be satisfactory if proper precautions are taken to preserve the alkaloids against decomposition by heat during the assay procedure.

Higher yields can be obtained by avoiding heat during evaporation of the solvents. The increase in yield by the U. S. P. method, using no heat in the evaporations is probably due, in part, to ammonia soaps extracted along with the alkaloids.

The use of a vacuum desiccator is suggested in order to hasten and facilitate evaporation at room temperatures.

LITERATURE CITED.

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(2) Markwell and Walker, *Chemist and Druggist*, 109 (1928), 525.

(3) Exler, *Pharm. Weekblad*, 65 (1928), 1152.
(4) Reindollar, JOUR. A. PH. A., 14 (1925), 789.
(5) Stikarofsky, *Ibid.*, 16 (1927), 30.

NOTE: The authors take this opportunity to thank Prof. E. D. Davy, School of Pharmacy of Western Reserve University, for his suggestions, criticisms and advice regarding this investigation.

THE PHARMACOGNOSY, CHEMISTRY AND PHARMACOLOGY OF VIBURNUM. III. HISTORY, BOTANY AND PHARMACOGNOSY OF VIBURNUM OPULUS L. VAR. AMERICANUM (MILLER) AIT.*

BY HEBER W. YOUNGKEN.

INTRODUCTION.

The American variety of *Viburnum Opulus* has been the theme of many contradictory discussions and reports within the past half century alike by botanists, pharmacognosists and pharmacologists. The purpose of this investigation, at least so far as the botanical and pharmacognic phases are concerned, is an attempt to straighten out this tangle first through historical studies and then by new research work upon authentic plants, representative specimens of which, including separated barks, have been permanently deposited in the herbarium of the Massachusetts College of Pharmacy.

Fig. 1.—*Viburnum Opulus* Linné **var.** *americanum* (Miller) Aiton. Shrub growing in Arnold Arboretum.

Detailed reports upon the chemistry and pharmacodynamics of the botanically standardized bark of this species will be published later by the collaborators on these phases of the investigation who are Florin J. Armhein (on chemistry) and James C. Munch (on pharmacodynamics).

HISTORY.

The taxonomic history of this plant takes us back to less than a decade before the American Revolution.

As early as 1768 Philip Miller in his Gardener's Dictionary (1) briefly described it as a distinct species which he named *Viburnum Americanum* or American Guelder Rose. He took

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cognizance of the European *Viburnum Opulus* or cranberry bush which he described separately on the same page referring to the description previously given it by Linnaeus.

In 1785, Humphrey Marshall in "Arbustrum Americanum" (2) named this plant *Viburnum trilobum* or Mountain Viburnum and described it as follows:

"This plant grows naturally upon mountains in the interior parts of Pennsylvania rising with slender stems to the height of 8–10 ft. The leaves are somewhat like those of the Guelder Rose or Snowball tree; they are narrowed at the base, but spreading and divided into three sharp pointed lobes, the middle ones longest and sometimes slightly toothed. The flowers are produced in the form of the others and are succeeded by berries of the same shape, of a pretty large size and a red color when ripe."

In 1789, Aiton in Hortus Kewensis (3) divided *Viburnum Opulus* into *V. opulus europea* α *ramulis viridibus opacis*, the Marsh Viburnum or Guelder Rose, β *Viburnum Opulus americana, ramulis rubicundis lucidis* or Red Twiged Viburnum or Guelder Rose and γ *V. opulus rosea*, the Snowball Viburnum or Guelder Rose. He thus took up Miller's species, *V. americanum* and reduced it to a variety of *V. Opulus* L.

Fig. 2.—*Viburnum Opulus* Linné **var.** *americanum* (Miller) Aiton. Leaf and flowering branch. Collected by H. W. Youngken at Framingham, Mass., May 20, 1929.

In 1803, Michaux in his "Flora Boreali-Americana" (4) described *Viburnum Opulus* as *V. foliis lobatis; petiolis glandulosis, cymis floribus sterilibus radiatis*. He recognized three varieties which he named **var.** α *europeanum*, β *Pimina* and γ *edule*. His Pimina variety was described as follows: "β *Pimina: foliis tricuspidatis; lobis sursum angustatis, promisee acuminatis.*" It corresponds to the common wild American plant.

In 1814, Pursh in his "Flora Americana Septentrionalis" (5) describes Aiton's *V. Opulus americanum* and Michaux's *V. Opulus Pimina* and Marshall's *V. trilobum* under the name of *Viburnum Oxycoccos*. He states that the berries are red and have an agreeable acid taste resembling that of cranberries, *Vaccinium macrocarpum*, for which he claims they are a very good substitute. In the 2nd edition of this same work (6) he states this variety is found in swamps, shady woods of Canada and on the mountains of New York and New Jersey.

Rafinesque (7) in Medical Flora (1828–30) points out that the bark of this *Viburnum* was used by the North American Indians as a diuretic usually in the form of a decoction, that some of the western tribes smoked the bark instead of tobacco and that the leaves of this and other species of *Viburnum* were employed as a tea by Indians and the early settlers.

In 1838, the same writer in his "Alsographia Americana" (8) readopted Michaux's *V. Opulus Pimina* for this plant, gave its distribution as from Ohio to Canada and described a form of this variety with subcordate leaves which he found in the Alleghanies of western Pennsylvania under the name of *Vib. Op. Pimina* **var.** *subcordatum* Raf.

In their "Illustrated Flora of the Northeastern U. S. and Canada" of 1913, Britton and Brown (9) describe the plant which Aiton called *V. Opulus americanum* and Marshall as *V. trilobum*

under the title of *V. Opulus* L., thus recognizing no distinction between the European and American species.

"Gray's Manual of Botany," 7th ed., revised by Robinson and Fernald (10), lists the American Cranberry-Tree under the section *Opulus* (Tourn.) DC. of the genus Viburnum as *Viburnum Opulus* L. var. *americanum* (Mill.) Ait. and calls it by the names or synonyms of Cranberry-Tree, High Bush Cranberry and Pimina. This work describes it in part as follows: "Nearly smooth, upright, 1–4 m. high; leaves 3–5 ribbed, strongly 3-lobed, broadly wedge-shaped or truncate at the base, the spreading lobes pointed, mostly toothed on the sides, entire in the sinuses; petioles bearing two glands at the apex; cyme broad, the marginal flowers neutral, with greatly enlarged flat corollas; stamens elongate." Its distribution is given as in woods and along streams from Newfoundland and Eastern Quebec to British Columbia, south to New Jersey, Pennsylvania, Michigan, Wisconsin and northeastern Iowa.

In 1927, Bush (11), discussing the taxonomy of some species of Viburnum calls attention to the earlier work of Blake and agrees with the latter that Miller's *Viburnum Americanum* rests on *Hydrangea arborescens*. He states in part: "It is quite apparent that Aiton intended to take up Miller's species americanum and reduce it to a variety under the European *V. Opulus* L. Even if he did not mention Miller as the author of the name americanum, and this being the case, the next available name for this species would be the *V. trilobum* Marshall, 1785."

In the same year in his "Manual of Cultivated Trees and Shrubs," Rehder (12) readopted the name of *Viburnum trilobum* Marsh. for the American variety of *Viburnum Opulus* thus giving it full species rank. In this same work he separately describes as a separate species the *V. Opulus* L. or European Cranberry Bark. A comparison of his two descriptions shows that this author bases his concepts for the elevation of the American variety to species rank mainly upon the longer, less toothed lobes of the leaves, shallow instead of narrow, grooved petiole and the small usually stalked glands instead of the large disk-shaped glands of the European species.

The more important events dealing with the morphologic and pharmacognic history has been largely discussed by the writer in the first article of this series (13). To this the following may be added: The bark of *Viburnum Opulus* was official in the seventh and eighth editions of the United States Pharmacopœia. The U. S. P. VIII (1905) gave a description which applied to Mountain Maple (*Acer spicatum*) bark.

Under the name of *Viburnum Opulus* or High Bush Cranberry Bark the bark of *Viburnum Opulus* L. var. *americanum* (Miller) Aiton became official in the National Formulary IV (1916). Here material which is apparently authentic is described as to physical characteristics, inner structure and powder.

It was continued as official in the National Formulary V (1926), this addition adding the synonym of Cramp Bark and describing the unground drug, structure and powdered drug and giving the list of official preparations into which it entered and the average dose.

The Homeopathic Pharmacopœia of the United States 3rd ed., revised 1914, page 581, recognizes as official the fresh bark of *Viburnum Opulus* including the bark of the root.

In his "Physiological Plant Anatomy," Haberlandt (14) calls attention to the fact that certain roots of Viburnum have cortical layers immediately outside of the endodermis furnished with thickening ridges forming a close to continuous mesh-work. He also states that in *V. Opulus* the inner walls of the cork cells are thicker than the others (15) and that the wood fibres very frequently are arranged in perfectly regular, radial rows (16).

Viehoever, Ewing and Clevenger (17) state that sclerenchyma fibres are usually absent in the secondary bark and are few and scattered in the primary cortex of young bark of *V. Opulus*, that the root bark of this species differs from the stem bark by showing almost an entire absence of stone cells and sclerenchyma fibres.

The earliest record of chemical studies upon *Viburnum Opulus* is that of Chevreul (18) who, in 1817, found valerianic acid in the European plant.

In 1844, Krämer (19) reported the presence in the European species of tannic acid, a bitter principle (viburnin), brown resin acid, chlorophyll, pectin, gum, wax, potassium malate, calcium malate, calcium sulphate, iron oxide and magnesia.

In 1900, Gibson (20) subjected the American *Viburnum Opulus* stem bark to proximate examination and found the air-dried drug contained 6.92% of moisture, 5.52% of ash, 87.56% organic constituents, 5.271% resin, 6.342% of waxy matter, 9.431% organic acids, 36.62% NaOH

extractive, 15.80% cellulose, 4.378% of colored extractive together with glucose and earthy phosphates and carbonates. He further stated that he believed the active principle to be a glucoside which he described of resinous character, greenish or greenish yellow in color, slightly soluble in water and completely soluble in alcohol.

In 1920, Clevenger and Ewing (21) analyzed the tree bark of American *Viburnum Opulus* and found the powdered drug to contain 10.7% total ash, 0.3% acid-insoluble ash and 11.04% of olive-green ether extract of which 1.14% was volatile with a characteristic valerianic acid odor.

By far the most extensive chemical examination upon the stem bark of the American Viburnum Opulus up to the present was that of Heyl (22) who in 1922 analyzed bark obtained through regular channels from northern Minnesota which conformed to the U. S. P. standards. He found the following substances: valerianic, acetic, caporic, caprylic, formic, oleic, linoleic, cerotic and palmitic acids, traces of paraffin, myricyl alcohol, phytosterolin ($C_{32}H_{56}O_4$), a phytosterol, an acidic resin readily yielding acetic and valerianic acids on hydrolysis and indications of the presence of a glucoside (by the Bourquelot method) which was not isolated. No alkaloid was found.

The same year Bemis (23) analyzed the fruit of this plant and found 2.92% of glucoside (viburnin), valeric acid, 0.19% oxalates, 0.16% citric acid, 0.81% malic acid, 6.65% sugar, 0.4% tannic acid and 3.45% of ash representing calcium phosphate and traces of potassium. He claimed that the valerianic acid and the glucoside exist independently of each other in that organ and that the acid did not form from the breaking down of the glucoside.

The history of the medicinal use of this plant dates back to the American aborigines of the time of Rafinesque (7) who reported them employing the bark as a diuretic.

The first account of its use in the practice of medicine was reported by Wooster Beach (24) in 1833.

King's "American Dispensatory" 18th ed. (25) states "Like *Viburnum Prunifolium* it is a remedy for the prevention of abortion and to prepare the way for the process of parturition. It allays uterine irritation with a tendency to terminate in hysteria, while in neuralgia and spasmodic forms of dysmenorrhoea it is a favorite remedy with many physicians."

According to W. Boericke (26), it is a general remedy for cramps, it often prevents miscarriage and is useful in the treatment of false labor pains and spasmodic and congestion affections of ovarian or uterine origin.

J. V. Shoemaker (27) in his "Materia Medica and Therapeutics" states the bark is used in the form of the fluidextract and is given to prevent cramps of all kinds resulting from hysterics, dysmenorrhoea or pregnancy.

In 1916 Pilcher (28) immersed longitudinal strips of the uterus (usually pregnant) in a bath of well-oxygenated Tyrode's fluid and tested the extract and infusion in strength of 1 : 1000 of the bark of *Viburnum Opulus* and *V. Prunifolium* upon these strips and recorded the contractions. He reported that *V. Opulus* produced slight depression and *V. Prunifolium* inconstant stimulation which he interpreted as practically negative results. Nothing is stated regarding the authenticity of the crude drugs used in the fluidextracts and infusions employed in his tests and the results he obtained are therefore of questionable scientific value.

Sollman (29) states that *Viburnum Prunifolium* and *Viburnum Opulus* enjoy the widest reputation among the uterine sedatives although their usefulness is no more demonstrated. He apparently bases his opinion upon the earlier work of Pilcher which he cites as evidence.

Wood (30) states that the berries of *V. Opulus* are antiscorbutic but that there is no sufficient reason to believe the bark has any medicinal properties of any kind.

In their "Essentials of Physiology and Pharmacodynamics," Bachman and Bliss (31) include *Viburnum Opulus* and *Viburnum Prunifolium* in the group of uterine sedatives and hemostatics and state that any action of these drugs on the uterus is questionable and the mechanism of action, if there be any, unknown.

Cohen and Githens in their Pharmacotherapeutics (32) claim that both *Viburnum Opulus* and *Viburnum Prunifolium* are much praised and also repeatedly stated to be without effect. That the fluidextract is given with apparent good effect in threatened abortion, that it may relieve pain and uterine contraction during pregnancy, that in dysmenorrhoea it acts by relieving spasm and congestion of the pelvic organs and that it is also given in subinvolution of the uterus

following pregnancy, as well as to quiet tearing after pains and to give tone to the uterus after the removal of one or more small fibroids. They express uncertainty of opinion as to all of these actions on account of the alcohol in the liquid preparations. They also state that there seems to be little difference in the action of the two forms of *Viburnum* and that the best preparations of either drug are the fluidextract and elixir.

It is quite evident from the foregoing citations that therapeutic opinion has been chaotic regarding the action of the bark of *Viburnum Opulus*. Search of the literature has failed to reveal any evidence that the particular bark used in preparations for the animal tests was botanically standardized. Moreover, it is clear that this drug as well as *V. Prunifolium* have been employed empirically with apparently good results.

MATERIALS AND METHODS.

The materials for this investigation consisted of entire shrubs of *Viburnum Opulus* L. **var.** *americanum* (Miller) Aiton and *Viburnum Opulus* L. growing in the

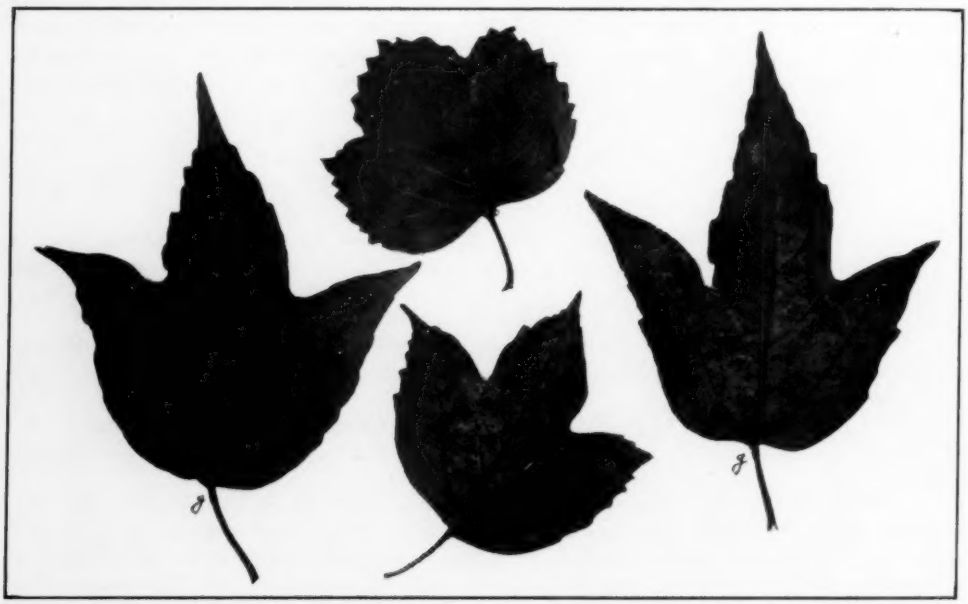

Fig. 3.—Types of leaves found on *Viburnum Opulus* Linné **var.** *americanum* (Miller) Aiton. Note petiole glands (g).

Arnold Arboretum and studied at various times during their growth and dormant periods by the writer, specimens of roots, stems, root and stem barks, leaf and flowering and leaf and fruiting branches gathered from these shrubs at various times during the spring, summer and autumn of 1927, 1929, 1930 and in the late spring of 1931, also of entire shrubs of *V. Opulus americanum* obtained from a nursery at East Boxford, Mass., and at Framingham, Mass., in May 1929, and compared with the Arnold Arboretum material and found to be authentic by the writer, also of 5 entire shrubs, 3 root systems and representative parts of aerial portion of the same plants and 50 lbs. of stem bark of *V. Opulus americanum* collected from authentic plants growing near Falmouth, Michigan, in late September and early October of 1930.

The methods employed by the writer in the investigation of the American variety of *Viburnum Opulus* were similar to those described under "Materials and Methods" in my earlier investigation of *Viburnum Lentago* (See JOUR. A. PH. A. 20; (1931) 315–317.

DESCRIPTION OF VIBURNUM OPULUS L. VAR. AMERICANUM (MILLER) AITON.

This plant commonly known as Cranberry Bush, Cranberry Tree, High Cranberry, High Bush Cranberry, American Cranberry Bush, American Guelder Rose and Pimina is an erect, nearly smooth, handsome shrub of open habit found in the woodlands and along streams from Newfoundland to British Columbia, south to New Jersey and Oregon and extending to Pennsylvania, and into Michigan, Wisconsin and Iowa, in many places of which it attains a height of 4 meters. Its stems are repeatedly dichotomously branched toward the summit and bear scaly winter buds. The trunk divides near the ground into two primary branches and these branch at successive levels typically in bifurcate fashion.

Its leaves are simple, opposite, petiolate, broadly ovate, palmately-3-lobed, broadly cuneate, rounded or truncate at base, up to 13 cm. long and 9.5 cm. in width, with lobes coarsely and irregularly toothed or nearly entire along the margin and acuminate at apex, the middle lobe being frequently elongated. The upper surface is dark green and glabrous, the lower surface pale green and pilose along veins. The venation is palmate-reticulate, the veins of the first order alternate. The petiole is up to 3 cm. long, grooved on upper surface with stalked to sessile glands at its apex and with a pair of elongated slender glandular stipules at its base.

The inflorescence is a stalked, broad, compound cyme bearing neutral marginal flowers and numerous minute, inconspicuous greenish fertile florets.

The fruit is a subglobular, scarlet drupe with a sour, succulent sarcocarp and a flat stony endocarp enclosing a single seed.

DESCRIPTION OF THE ROOT BARK.

The root bark occurs in short pieces or chips, externally dark brown to purplish brown, irregularly longitudinally wrinkled, reddish brown where cork is abraded, scaly on older roots and nearly smooth on younger roots. The fracture is short, very brittle and uneven, the fractured surface exhibiting a brown outer bark and a whitish middle and inner bark. The odor is indistinct in bark which has been stored for some time but becomes strongly valeric-acid like when the bark is triturated with phosphoric or hydrochloric acids. Odor of freshly gathered drug is very strongly valeric-acid like. The taste is bitter and slightly astringent.

When 0.5 Gm. of ground root bark was boiled with 20 cc. of distilled water and filtered, a very pale brown colored clear filtrate resulted. When a portion of this filtrate was treated with 4 drops of a 2% $FeCl_3$ solution, a dark green mixture resulted. When this was filtered, the filtrate was a clear green and the precipitate dark green to greenish-black. When a second portion of the first filtrate was treated with ammonium molybdate T. S. (U. S. P.), a yellowish color resulted with the separation of a dirty yellow precipitate.

When the inner surface of the root bark was treated with a 2% solution of $FeCl_3$ a blue-green color resulted.

HISTOLOGY OF THE ROOT.

Piliferous Region.

Cross sections through the root a very short distance above the cap exhibit the following structures:

1. Epidermis of large polygonal to slightly radially elongated cells with thick outer cuticle and clear contents, a number of the cells being extended into short papillæ and root hairs.

2. Primary Cortex of 4 to 5 layers of rounded to polygonal parenchyma cells and small angular air spaces.

3. Endodermis, of ellipsoidal outline, the poles of the ellipse being marked by cells with thick, brownish walls.

4. Pericambium of a layer of small, thin-walled cells.

5. Radial fibrovascular bundle consisting of an oblong strand of xylem flanked on either side by an elongated strand of phloem.

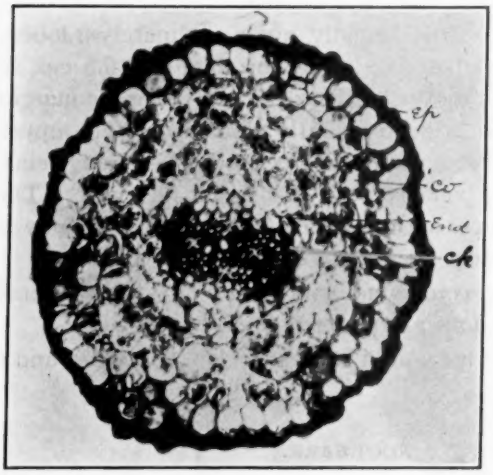

Fig. 4.—Photomicrograph of a cross section of the root of primary growth of *Viburnum Opulus* var. *americanum* showing a diarch bundle in the center of the illustration. × 52. *ep*, epidermis; *co*, primary cortex; *end*, endodermis; *ck*, early appearance of cork; *x*, xylem strands and *pr*, phloem strands of a diarch radial fibrovascular bundle.

Six Inches from Tip.

1. Epidermis with radially-elongated epidermal cells having a thick cuticle.

2. Primary cortex of 5 to 6 layers of rounded to tangentially elongated cortical parenchyma cells and small angular air spaces.

3. Endodermis of tangentially elongated endodermal cells, the radial walls of which are not averagely thicker than the outer or inner walls.

4. Pericambium which has divided into outer and inner layers and begun to lay down cork in the interrupted patches, of a single layer in thickness.

5. Protophloem of soft bast. The secondary phloem has begun to be laid down. An interfascicular cambium has formed which has already tagged on to the intrafascicular cambium and formed a complete cambium ring. Four primary xylem strands are evident. These have been somewhat deepened by a secondary xylem having been laid down on their outer faces.

6. Pith, beginning to be crushed out.

Eleven Inches from Tip. (*Early Secondary Growth.*)

Section cut through this region show: (*1*) an epidermis which has almost completely sloughed off, having been replaced by 6 or 7 layers of cork, (*2*) a phellogen in the state of division, (*3*) secondary cortex of about 4 layers of parenchyma cells and

air spaces, (*4*) a circle of open collateral bundles separated by narrow medullary rays which are 1 cell in width. Each bundle shows about 5 layers of phloem, a distinct cambium and a broad xylem wedge which in radial longitudinal section exhibits tracheæ with scalariform and oval bordered pore markings together with elongated xylem cells and wood fibres with attenuated ends.

Root of Medium Thickness.

Sections through a portion of the root of 2 years of age exhibited further secondary increase in thickness. The cortex and phloem were somewhat broader. Rifts had begun to appear in cortex and small sclerenchyma patches were evident in protophloem and outer cortex. Rosette aggregates of calcium oxalate were observed in a number of cells of the cortex and phloem. The pith had become completely crushed out.

In surface view the cork cells were polygonal to somewhat tangentially elongate up to 106.20μ × 56.64μ. In cross sections the cork cells measured were up to 70.8μ × 17.7μ.

Sections through portions of a root 3 years of age showed tabular cork cells which in cross sections were occasionally up to 85.53μ × 28.32μ and frequently to 70.8μ × 17.7μ. Many of the cork cells slightly lignified and showed evidence of vertical thickenings in their walls. In surface sections the cork cells appeared irregularly polygonal and were up to 106.20μ × 63.72μ.

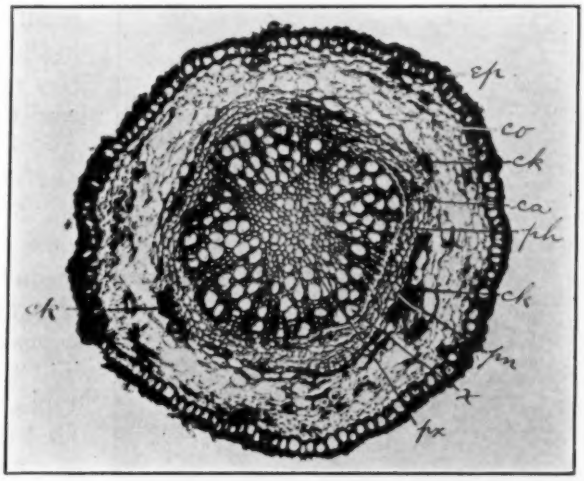

Fig. 5.—Photomicrograph of a transverse section of the root of early secondary growth of *Viburnum Opulus* **var.** *americanum*, cut 6 in. from tip, × 52, *ep*, epidermis; *co*, primary cortex; *ck*, cork cut off by a phellogen originating from division of pericambium; *pn*, cork cambium; *ph*, phloem; *ca*, cambium; *x*, secondary xylem; *px*, primary xylem.

The medullary rays were 1 to 2 cells in width. Occasional groups of stone cells were evident in the phloem.

The xylem wedges were deeper than in the younger sections studied and showed numerous scalariform tracheæ, fewer pitted tracheæ and many wood fibres, the latter arranged in radial rows.

Calcium oxalate crystals were numerous in the cortex and phloem occurring as rosette aggregates usually from 15μ to 25μ but occasionally up to 35μ in diameter.

Old Thick Root.

Sections cut through older portions of the root showed the following structural peculiarities:

1. Cork of numerous layers of tangentially-elongated cells with lignified walls.

Many of the cork cells were up to 70.8μ long $\times$ 21.24μ in breadth, a few up to 120.75μ $\times$ 41.4μ when examined in surface view.

2. Phellogen of tangentially-elongated meristematic cells.

3. Secondary cortex of several layers of tangentially elongated parenchyma cells most of which have starch or rosette aggregate-crystal contents, a few having brownish contents.

4. Phloem, a broad zone traversed by numerous phloem portions of medullary rays which are mostly 1 cell wide but up to 2 cells in width and vary in their path from straight to curved, forming convergent groups in places.

Fig. 6.—Photomicrograph of a cross section of the root bark of *Viburnum Opulus* var. *americanum* obtained from the oldest portion of a root, $\times$ 77, *b*, borke; *ck*, cork tissue; *pn*, a secondary phellogen; *ph*, phloem; *cr*, rosette aggregate of calcium oxalate; *mr*, phloem medullary ray; *st*, group of stone cells in phloem.

Scattered groups of stone cells and small islets or individual stone cells occur in the phloem, some intercepting medullary rays. The largest groups observed were up to 340μ $\times$ 170μ.

5. Cambium, wavy in outline, or meristematic cells.

6. Xylem, a broad porous, radiate zone traversed by xylem portions of medullary rays which separate numerous elongated wood wedges that are chiefly composed of straight rows of wood fibres and tracheæ of scalariform and pitted types. The medullary rays of the xylem are 1 to 2 cells in width.

The starch grains occurring in the parenchyma cells were simple, spheroidal, subspheroidal to occasionally ovate or 2-3 compound, more rarely up to 4-5 compound, the simple grains up to 10.62μ in diameter, some with distinct central, rounded to cleft hilum. The rosette aggregate crystals of calcium oxalate were up to 38μ in diameter but mostly up to 25μ.

POWDERED ROOT BARK.

The bark powdered was removed by the writer from a root system of an entire shrub growing near Falmouth, Michigan. It was passed through a No. 60 sieve. Both mill and sieve were thoroughly cleansed before the operation.

The powdered drug was grayish brown and exhibited the following histological elements: Numerous rosette aggregates of calcium oxalate from 10.62μ to 38μ in diameter together with angular to deltoid fragments of these crystals; numerous starch grains which were simple, spheroidal to ovoid and 2- to 3-compound, rarely up to 4- to 5-compound, the individual grains often showing a central spheroidal, angular or curved hilum and up to 10.62μ in diameter or length; numerous fragments of starch and crystal parenchyma, some cells of which contained

brownish amorphous contents; fragments of brownish cork with irregularly polygonal to rectangular shaped cells whose walls were more or less suberized to lignified, many with unevenly thickened walls, frequently up to 70.8μ x 28.32μ, occasionally up to 120.75μ x 41.4μ; stone cells of various shapes with lignified walls and prominent pore canals, up to 217.4μ x 53μ; few fragments of sclerenchyma fibres with walls thicker than lumen and giving a pink color with phoroglucin and HCl.

DESCRIPTION OF STEM BARK.

The bark of the stem occurs in strips, quills or chip-like fragments usually up to 1.5 mm. in thickness but occasionally up to 3 mm. As examined on the entire shrub allowed to dry in the laboratory, it was purple on young thin twigs, greenish to greenish brown or greenish yellow on young portions of main shoots and irregularly longitudinally wrinkled. Passing downward for a distance the next older bark was grayish brown with areas of silvery (light gray) lustre. Still older bark was grayish black to blackish and greenish to light brown to brown where abraded.

The lenticels were slightly raised, ovoid, circular to elliptic in shape and arranged both transversely and longitudinally. They were numerous in middle aged and older stem portions. The old bark toward the base of the stem displayed irregular brownish areas, many circular stem scars and cork exfoliating in this area.

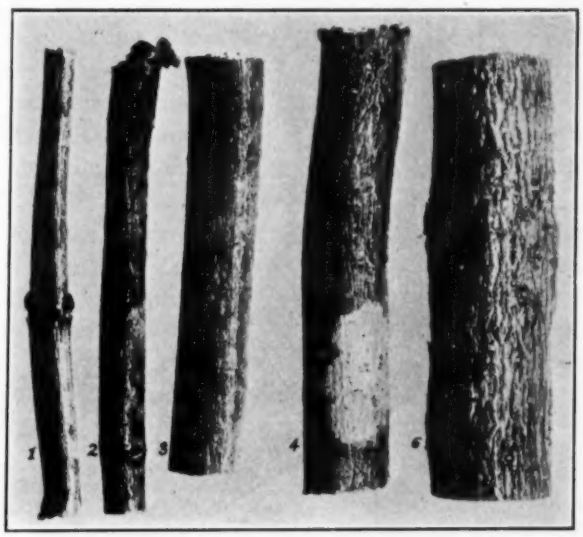

Fig. 7.—Stem bark of *Viburnum Opulus* Linné **var.** *americanum* (Miller) Aiton obtained from an entire shrub growing near Falmouth, Michigan. The numbers refer to successive year's growth of the stem from which the bark was taken.

The inner surface varied from greenish yellow to yellowish to rusty brown and was irregularly transversely to obliquely or longitudinally striated. The transverse and oblique striae were undulate. The fracture was short and weak, the fractured surface showing a brown to rusty brown outer bark, a greenish phelloderm and pale brown to yellowish inner bark. The odor of the dried bark was slight and characteristic but became strongly valeric-acid like upon trituration in a mortar with phosphoric or hydrochloric acid. The taste was bitter and moderately astringent.

When the inner surface of the stem back was treated with a 2% solution of $FeCl_3$, a dark green color resulted changing to black on drying.

When 0.5 Gm. of ground stem bark was boiled with 20 cc. of distilled water and filtered, a very pale yellow, clear filtrate resulted. When a portion of this filtrate was treated with 4 drops of a 2% solution of $FeCl_3$, a precipitate resulted which, when separated by passing the mixture through filter paper, was dark green to greenish

black while the filtrate was green. When to the second fraction of the first filtrate 2 drops of ammonium molybdate T. S. (U. S. P.) was added, a deep yellow color resulted. Both young and old stem barks were tested as above with similar results.

HISTOLOGY OF THE STEM.

A series of sections were studied which were cut through successive levels of the

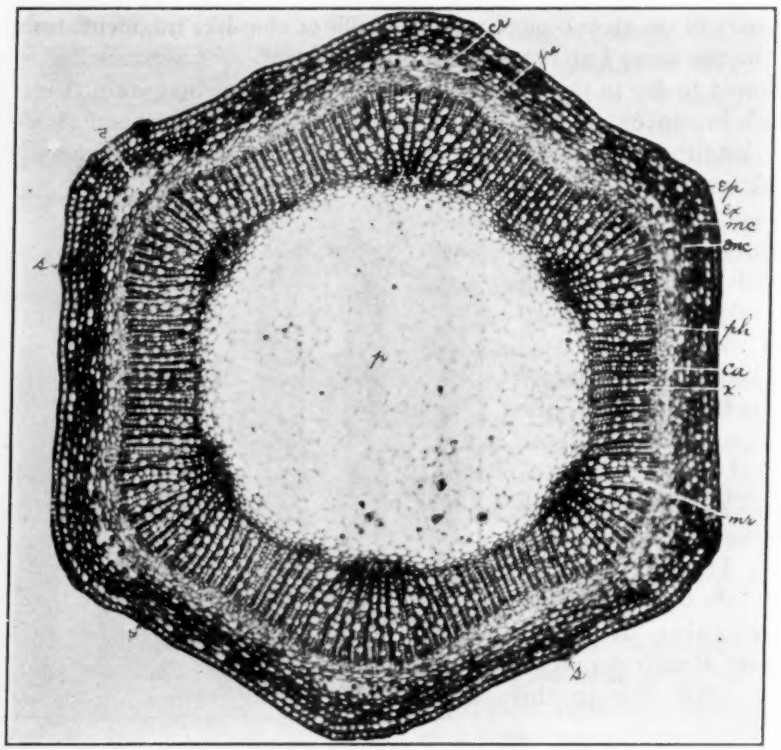

Fig. 8.—Photomicrograph of transverse section of stem of *Viburnum Opulus* var. *americanum* cut directly beneath terminal bud, × 52. *ep*, epidermis; *s*, stomata; *ex*, exocortex; *mc*, mediocortex; *enc*, endocortex; *pe*, pericycle; *ph*, phloem; *ca*, cambium; *x*, secondary xylem; *px*, primary xylem; *r*, right; *cr*, rosette aggregate of calcium oxalate; *p*, pith; *mr*, medullary ray in xylem.

stem starting just beneath the terminal bud and proceeding downward toward the base.

A. Just below Terminal Bud. (Early First Year Growth.)

The cross section was 6-angled with rounded angles. The following structures were noted:

1. Epidermis of rounded to slightly tangentially elongated cells with cutinized outer walls and scattered stomates. In regions of stem angles the epidermal cells tend to become radially elongate with convex outer walls.

2. Primary Cortex of 5 to 6 layers of largely chloroplastid containing cells consisting of an outer hypodermis or exocortex of more or less collenchymatous cells

which tend to be larger than most of the subjacent layers of the cortex, the latter being mostly parenchymatous. Rifts occur in the inner part of the mediocortex and are always seen in the angle regions where they harbor a number of rosette aggregates of calcium oxalate. Smaller rifts occur elsewhere in the cortex and pericycle. In the angle regions the cells of both exocortex and mediocortex (beyond the rifts) are collenchymatous. The endocortex (endodermis) is composed of a layer of parenchyma cells of averagely large size. Some of the outermost layer of cells of the cortex (hypodermis) show division through formation of a tangential wall through center (early formation of phellogen).

3. Pericycle of parenchyma cells resembling those of the endocortex. Here and there are to be noted the beginning of pericyclic fibers as isolated modified cells with empty lumen and clear glistening walls which show thickening.

4. Primary Phloem, a narrow zone of sieve tubes and phloem cells, traversed by narrow phloem medullary rays.

5. Cambium, 6-angled and composed of meristematic cells. The intrafascicular cambium had already been laid down.

6. Xylem. Broadest in regions of stem angles and showing numerous, narrow wood wedges composed of tracheids, wood fibres, scalariform and pitted tracheæ separated by narrow medullary rays.

7. Pith, a broad zone of thin-walled, pitted parenchyma cells and angular air spaces. Some of the pith cells contain rosette aggregates of calcium oxalate, a few monoclinic prisms, others spheroidal starch grains up to 10.62μ in diameter. In 50% alcohol mounts a number of the pith cells contain brownish sphæro-crystals, a few colorless rhombohedral crystals. Some of the cells of the conjunctive tissue surrounding the pith also show this last type.

The maximum thickness of the bark was 49.56μ, of the xylem 63.72μ.

Two Inches below Terminal Bud. (First Year's Growth.)

The outermost layer of cells of the cortex (hypodermis) has already divided to form a phellogen which by this time has cut off 3 to 4 layers of young cork cells on its outer face beneath the epidermis. Some of the young cork cells show crystalline contents when examined in alcohol mounts. The cells throughout the mediocortex have become collenchymatous. Rosette aggregates of calcium oxalate have made appearance in the phloem. Single sclerenchyma fibers and small groups of 2 or 3 usually occur at wide intervals in the pericycle. The contour of the margin of the stem and of the cambium is less angular. The xylem has been deepened through deposition of secondary xylem on the inner face of the cambium ring. The maximum thickness of the bark was 70.8μ, that of the xylem 106.2μ.

Five Inches from the Terminal Bud. (First Year's Growth.)

Cross section are practically circular in outline. The bark region had a maximum width of 416.5μ, the xylem 500μ.

The epidermis was still present but many of its cells contained air and were nearly ready to sluff off.

The subepidermal cork zone had been augmented by an additional layer or two of cork.

The phloem, pericycle and inner cortex regions showed an increased number of rosette aggregate crystals of calcium oxalate. The pericycle showed a few additional pericyclic fibres. The protophloem showed an occasional bast fibre with thick walls and narrow lumen. The pericyclic fibres were up to 31.86μ in width, the rosette aggregates up to 26.5μ. The cambium line was wavy in outline. The xylem showed considerably more secondary wood than in the previous section.

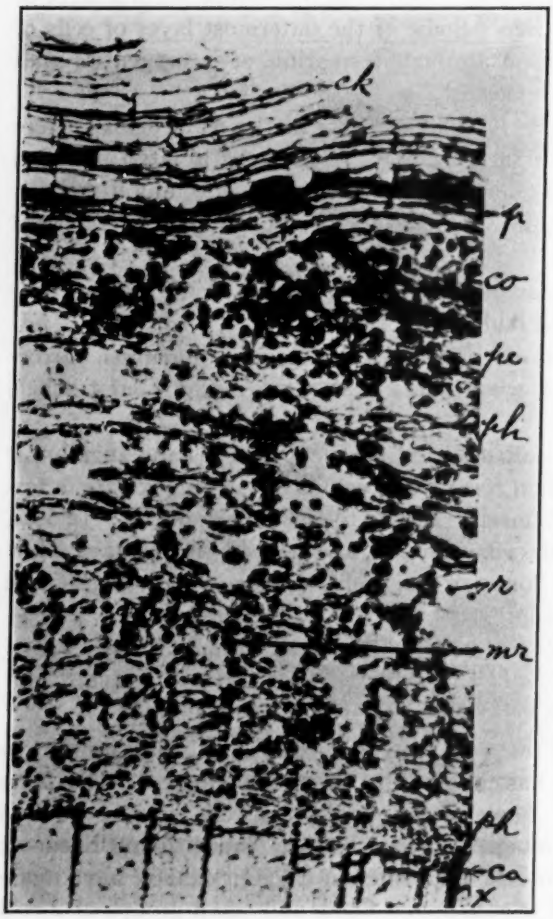

Fig. 9.—Photomicrograph of a cross section of the five-year stem bark of *Viburnum Opulus* var. *americanum*, × 80. *ck*, cork; *p*, phellogen; *co*, cortex; *pe*, pericycle; *ph*, phloem; *mr*, medullary ray; *r*, rosette aggregates of calcium oxalate.

Eight Inches from Terminal Bud. (Second Year's Growth.)

Cross sections were circular in outline. Maximum width of bark was 450.5μ, of xylem 1983μ.

The epidermis was in the process of exfoliation. The bark showed but slight increase in thickness over previous sections (34μ), but the xylem had increased materially in diameter. It showed wood fibres with bordered pores and scalariform and pitted tracheæ when examined in radial longitudinal section.

The pericyclic fibres and bast fibres showed increase in thickness of their walls, some fibres being up to 45μ in diameter.

Twelve Inches below Terminal Bud. (Three Year's Growth.)

Maximum thickness of bark 749.7μ, of xylem 2918μ. The epidermis has completely disappeared together with some of the outer cork layers. The walls of the cork cells have become suberized and to some extent lignified. Many of the cork cells show the greater thickening on their inner walls. They varied from 17.7μ to 71.8μ in length × 10.62μ to 24.78μ in width in cross sections and longitudinal radial sections.

The xylem elements showed increased lignification. The medullary rays were 1 to 2 cells wide in tangential longitudinal sections. Radial longitudinal sections showed occasional non-lignified pericyclic fibres but these were not seen in every section. A number of crystal fibres with rosette aggregates as well as isolated rosette aggregates occurred in the phloem and pericycle.

The tracheæ in cross sections were mostly arranged singly and in groups of 2, more rarely in groups of 3. The wood fibres in such sections occurred in radial rows. Some of the conjunctive tissue cells showed considerably lignification of their walls as observed in radial longitudinal sections.

The sections through the several successive regions of the stem so far discussed will serve to illustrate progressive steps in the development of the stems of this plant. All of them showed a bark which is similar to authentic commercial samples designated as "Young Cramp Bark."

Seven Feet below Terminal Bud. (Five Year's Growth.)

Maximum thickness of bark 1322μ: width of xylem 6.5 to 8.5 mm. Transverse sections show an outer zone of fissured cork of up to 8 or 9 layers of tangentially elongated cork cells whose inner walls are considerably thickened and lignified, the thickenings being irregularly wavy in character. These cells measured up to 95μ × 39μ. A phellogen, a cortex and pericycle of about 20 layers of tangentially elongated to rounded parenchyma cells and spaces in which regions are to be found many rifts. The parenchyma cells contain either rosette aggregates of calcium oxalate, minute starch grains or amorphous yellowish brown contents. Pericyclic fibres, as in the previous growth of the stem were only occasional and not seen in the majority of sections studied.

The phloem was broad and traversed by numerous medullary rays 1–2 cells wide which ran straight in some regions but tended to curve and converge in groups in their outer path. No bast fibres were observed in the phloem patches. Rosette aggregates of calcium oxalate were abundant in the phloem cells. The medullary ray cells had pitted walls and prominent large nuclei. The calcium oxalate crystals were up to 38.9μ in diameter being mostly under 35μ.

As in the previous sections the xylem showed the wood fibres largely arranged in radial rows. Radial longitudinal sections showed occasional non-lignified pericyclic fibres, numerous crystal fibres containing rosette aggregates in pericycle and phloem. The xylem in these sections showed scalariform and pitted tracheæ and tracheids as well as wood fibres with simple oblique pits and with bordered pits. Tangential sections showed the medullary rays to range from 1–2 rows of cells in width. The starch grains found in the phloem cells were spheroidal, ovate or ellipsoidal with central hilum and up to 14μ in diameter.

Stem of Six Year's Growth.

The microscopical features of these sections resembled those of the 5-year stem except that we note here the first occurrence of stone cells in the phloem. These are of a variety of shapes and sizes with lamellated walls showing varying degrees of lignification. Many are more or less isodiametric, others elongated and a number quite fibre-like but showing pore canals.

Cross sections cut at further levels downward show secondary phellogens arising in cortex, pericycle and outer phloem causing a sluffing off of the primary bark tissues. This accounts for the presence of pericyclic fibres and a moderate number of bast fibres in the young bark of commerce and their almost complete absence in commercial older barks.

HISTOLOGY OF OLD STEM BARK (10 YRS. OLD).

Sections were cut through the basal portion of the stem adjoining the root. The xylem of these showed 10 annual rings. The bark portion had a thickness of 1500μ.

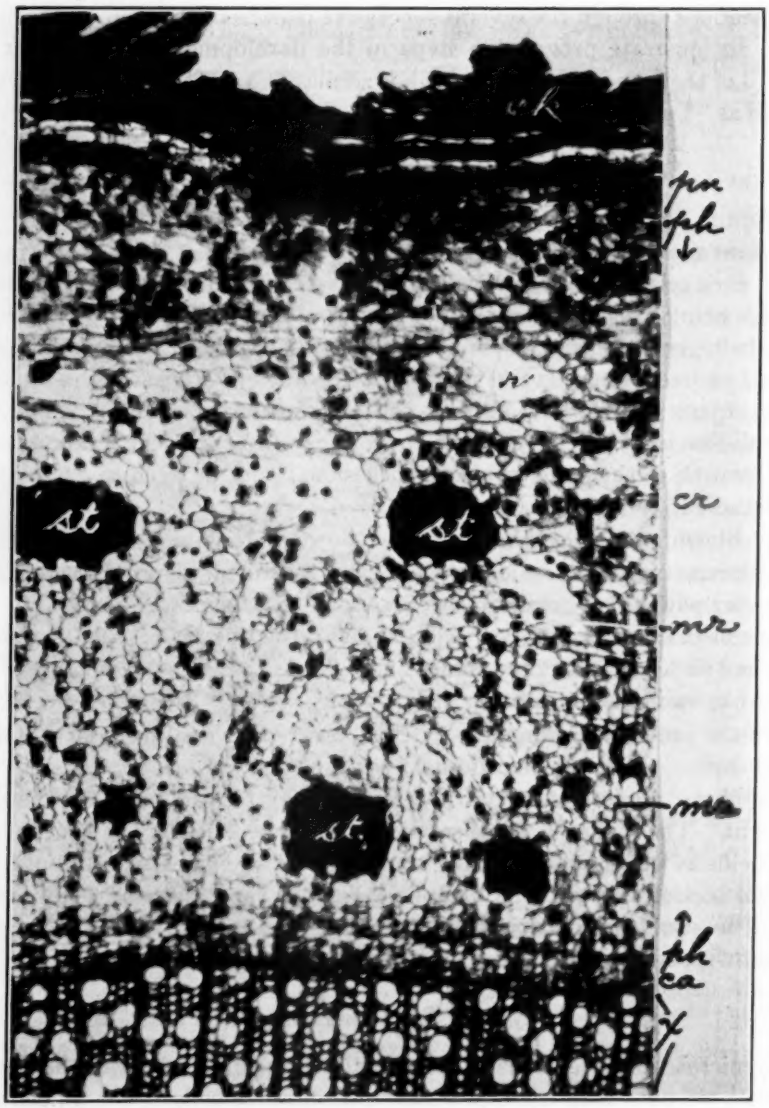

Fig. 10.—Photomicrograph of old stem bark of *Viburnum Opulus* var. *americanum* with adherent wood, as seen in cross section, × 81. *ck*, cork; *pn*, secondary phellogen; *ph*, phloem; *cr*, rosette crystal of calcium oxalate; *mr*, medullary ray; *ca*, cambium line; *x*, xylem; *r*, rift between parenchyma cells of phloem; *st*, groups of stone cells.

These sections showed a complete absence of cortex and pericycle. The following bark structures were noted passing from periphery to center:

1. Outer phloem region of dead cells or completely exfoliated in some sections.

2. Several layers of tabular cork cells whose tangential walls are for the greater part both suberized and lignified. While the radial walls of most of the cells observed were suberized, a few show lignification. Many of the cork cells showed ridge-like thickenings in their walls. The cork cells varied from 17.7μ to 95.5μ in length and from 10.62μ to 35.4μ in breadth.

3. A secondary phellogen of clear-looking meristematic cells in the process of division.

4. A broad secondary phloem separated into a number of irregularly oblong phloem patches by numerous medullary rays which run nearly straight in the inner region but which for the greater part pursue curved courses in the outer portion of the phloem. Most of the phloem patches consist of starch- and crystal-containing phloem parenchyma and sieve tubes but scattered here and there and intercepting medullary rays were observed some groups of sclerenchyma consisting of stone cells of variable size and shape some of which are elongated and fibre like.

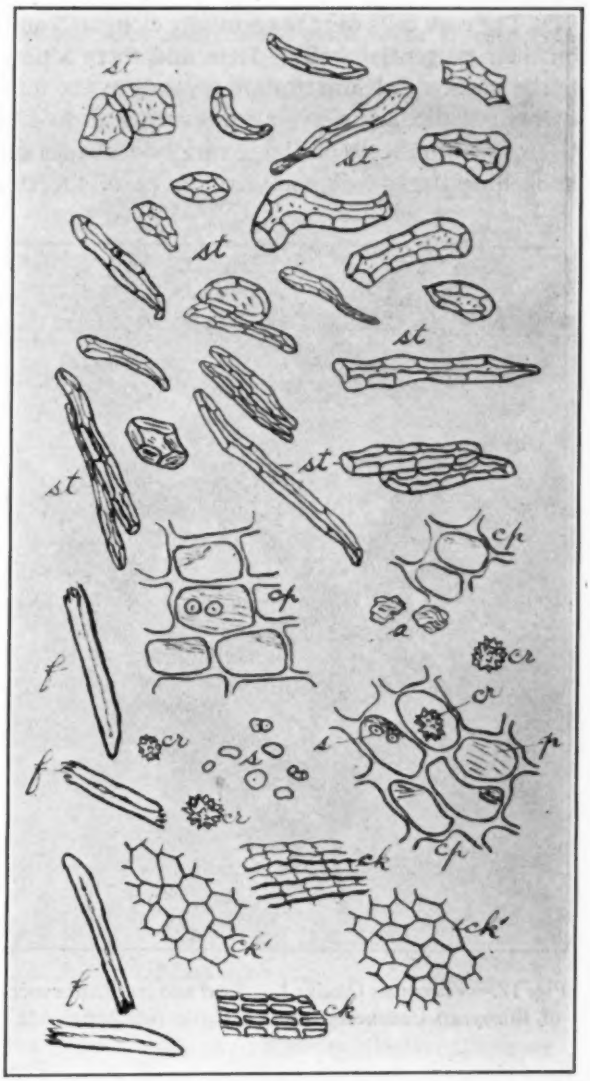

Fig. 11.—Powdered *Viburnum Opulus* var. *americanum* stem bark. *st*, stone cells; *cp*, cortical parenchyma; *a*, resinous material occurring in parenchyma of bark; *s*, starch grains; *cr*, rosette aggregates of calcium oxalate; *f*, pericylcic fibers from young bark; *ck*, cork tissue in transverse section; *ck*, cork tissue in surface view.

The sclerenchyma groups are for the greater part widely scattered but occasionally are found fairly close, never however as numerous as in the older *Acer spicatum* stem bark. A few isolated stone cells are also present. In some sections the groups assumed a tier-like arrangement but, unlike the sclerenchyma fibres of *Acer spicatum* bark, had broad intervening spaces of soft bast between the series of groups.

A striking feature of these sections was the great abundance of rosette aggregates of calcium oxalate.

Radial-longitudinal sections showed many cells in the outer phloem with brownish to reddish contents and thick lamellated walls. These in some places were disposed in groups, the groups appearing collenchymatous.

The cork cells were tangentially elongated and for the greater part were lignified on their tangential walls. Here and there a pericyclic fibre was imbedded in the borke mass. Calcium oxalate crystals in the form of rosette aggregates were very numerous, the larger crystals measuring up to 42.48μ in diameter. Most were up to 35.4μ. Stone cells of a large variety of shapes and thickenings occurred, some with hooked and crenated margins. Some of the stone cells were elongated and appeared like fibres but usually showed distinct pore canals. The stone cell groups measured were up to 1499μ in length and up to 416.5μ in width.

Fig. 12.—*Viburnum Opulus* L. Leaf and fruiting branch of European Cranberry bush × 1/2; g. petiolar glands.

The medullary rays traversed the other elements at right angles, their cells showing thick porous walls and starch, tannin or rosette crystals, occasionally reddish brown contents.

Tangential-longitudinal sections exhibited numerous medullary rays 1 cell in width and a scattering of others 1–2 cells in width, more rarely in some sections a medullary ray is seen 1–3 cells wide. In this type of section the medullary ray cells appear rounded ovate to ellipsoidal. The stone cell groups were up to 1450μ in length and up to 416.5μ in width. Some isolated stone cells of variable outline were also seen. The cork cells appear tangentially elongated and many show lignification on their tangential walls. Numerous crystal fibres containing rosette aggregates of calcium oxalate are present as well as isolated rosette aggregates, the latter occurring in many of the parenchyma and medullary ray cells.

POWDERED STEM BARK.

The powders studied were those of barks picked from young and older portions of stems of shrubs collected at Falmouth, Michigan, and from the same lot of plant material used in the description of the foregoing sections. The bark was carefully deprived of adherent wood and ground in a previously cleansed mill and passed through a 60-mesh sieve.

They were light grayish brown in color and showed the following elements: Numerous fragments of starch- and crystal-parenchyma and medullary ray cells, the latter with beaded

walls; starch grains mostly small, somewhat less numerous than in the root bark and frequently adherent to walls and dead protoplasm of parenchyma cells, the grains spheroidal to ovoid, very small and usually not exceeding 6μ; a few thick walled pericyclic fibres; numerous fragments of brownish cork tissue with cells of polygonal or tabular outline, the latter usually in layers and showing thickened tangential and occasionally radial walls, walls of cork cells suberized to lignified; the polygonal cork cells usually up to 70.8μ × 35.4μ, the tabular up to 106.20μ in length and up to 35.4μ in width; stone cells of a variety of shapes and degrees of lignification up to 124μ long and 35.4μ in breadth; numerous rosette aggregates of calcium oxalate up to 42.48μ in diameter; a few fragments of adherent wood elements (practically unavoidable in preparation) consisting of lignified wood fibres with oblique and bordered pits and scalariform and pitted tracheæ.

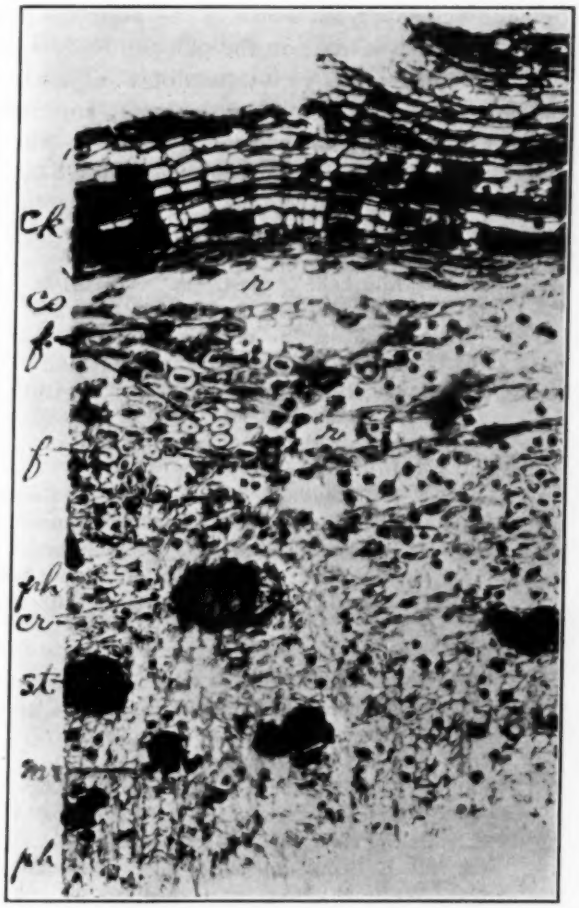

Fig. 13.—Photomicrograph of a cross section of 5-year stem bark of *Viburnum Opulus* (European species). × 80. *ck*, cork; *co*, cortex; *f*, sclerenchyma fibres in pericycle; *ph*, phloem; *st*, groups of stone cells; *mr*, medullary ray in phloem; *r*, rifts between parenchyma cells; *cr*, rosette aggregates of calcium oxalate.

DISTINCTIONS BETWEEN VIBURNUM OPULUS VAR. AMERICANUM AND VIBURNUM OPULUS (EUROPEAN).

For this purpose the writer compared shrubs of both the American and European *V. Opulus* plants growing in adjacent plots in the Arnold Arboretum, herbarium sheets of both kinds of plants grown in Europe and America and sections of stems of the same age collected from American and European varieties with the following results:

The petiolar groove of *V. Opulus* var. *americanum* is more flattened and open whereas that of *V. Opulus* is narrow and often closed to the very top. When the petiole of *V. Opulus americanum* dries up and shrivels, the groove becomes narrower, hence this difference is best noted on fresh material.

The petiolar glands (at apex of petiole) of *V. Opulus* var. *americanum* are smaller and more numerous whereas those of *V. Opulus* are fewer (usually only 2) and larger.

The fruits of *V. Opulus* var. *americanum* are short ellipsoidal and averagely slightly larger whereas the fruits of *V. Opulus* are subglobose, averagely somewhat

smaller. The former are edible and devoid of the bitter taste which characterizes the fruits of the latter.

The stem of the 5th year's growth of *V. Opulus americanum* usually possesses very few non-lignified sclerenchyma fibres in the pericycle and few or no stone cells in the phloem whereas that of *V. Opulus* shows many small groups of non-lignified sclerenchyma fibres in the pericycle and numerous groups of stone cells and some isolated ones in the phloem.

The cork of this year's stem of *V. Opulus americanum* possesses more layers showing lignified thickening of the inner tangential walls than that of European *V. Opulus*. The cork of the latter tends to have alternate zones of non-lignified cells between zones showing lignification.

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MASSACHUSETTS COLLEGE OF PHARMACY, BOSTON.

ALKALOIDAL REAGENTS. III. PROPADRIN, ITS HOMOLOGS AND DERIVATIVES.

BY JAMES C. MUNCH, FRANK C. CROSSLEY AND WALTER H. HARTUNG.*

Continuing the study of the seventeen commoner alkaloidal reagents (5), the reactions were determined with epinephrine, ephedrine and various analogous amino-alcohols synthesized in these laboratories (2, 3, 4). The results are given in the seven accompanying tables. Discounting the results with Reagent No. 12 (potassium permanganate), in which the precipitate is probably manganese dioxide (5), there is nothing unusual in the data obtained. None of the arylalkanolamines give a color reaction except *B*-naphthylpropanolamine (Table I), and it appears that this color is characteristic for this compound. The precipitate reactions (Table I) show nothing characteristic, except that as the molecular weight increases an increasing number of reagents give positive tests. It is not unlikely that if stronger original concentrations of the compounds tested had been employed, more precipitates would have been obtained. That is, these results are probably indicative of the solubility rather than of characteristic responses. The positive reactions with Reagent No. 5 (mercuric potassium iodide) indicate that it is the most sensitive of these reagents. The phenolic derivatives (Tables II and III) are much more sensitive, but the difference between position isomers becomes less marked than one would expect from similar tests with phenol and cresols (6). The positive color test of Reagent No. 15 (uranium acetate) with *m-p*-dihydroxypropadrin, and the negative result with its isomer, epinephrine, appears most characteristic.

The methyl ethers of the phenolic derivatives of propadrin (Tables IV and V) are less sensitive than the phenols themselves, yet more sensitive than propadrin.

There appears to be no substantial difference between the sensitivity of the amino-alcohols and the corresponding amino ketones (Tables VI and VII), as indicated by the behaviour with any single reagent.

It may not be amiss to point out that the data obtained thus far in no manner shed any light on the physiological idiosyncracies of a homologous series, such as has been prepared and studied in these laboratories (1).

SUMMARY.

The behaviour of seventeen alkaloidal reagents with a series of epinephrine and ephedrine-like compounds has been observed, and the results have been summarized in tabular form.

BEHAVIOR OF SEVENTEEN ALKALOIDAL REAGENTS WITH PROPADRIN AND DERIVATIVES.

TABLE I.—HYDROCARBON AROMATIC NUCLEI.

For key and abbreviations see April 1932, page 341, *et seq.*

Product.	Precipitate Formation. Reagent Number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Phenyl-ethanol-amine					*y*							*b*					
Propadrin (phenylpropanol-amine)												*b*					
Phenylbutanolamine												*b*					

* Research Laboratories, Sharp & Dohme, Inc., Philadelphia, Pa.

TABLE I—*Continued.*

Product.	Precipitate Formation. Reagent Number. 1.	2.	3.	4.	4.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Phenyl-pentanol-amine					*w*	**w**						*b*			*w*		
Phenyl-hexanol-amine	*w*	*w*			*yw*				*y*			*b*			w		*w*
Phenyl-octanol-amine	w	w			W	w	b		*y*		*y*	*w*	*b*	*y*	*W*		w
p-Methyl-propadrin (*p*-tolyl-propanolamine)					yw										*w*		
p-Phenyl-propadrin*	w	w	w	w	w	w	rb	y	y		y	w	b	yw	w	w	w
a-Naphthyl-propanolamine		*w*	*w*		*w*	*w*	*rb*	*y*				w	b	y	w	*w*	*w*
b-Naphthyl-propanolamine		*w*	*w*		*w*	*w*	*rb*	y				*w*	*b***	*y*	w	*w*	*w*
Ephedrine (phenylpropanol-methylamine)					*yw*		*b*						*b*				*Y*

* Saturated solution.

** Gives *rb* color with reagent 12; remainder failed to show color reactions.

TABLE II.—PHENOLIC DERIVATIVES.

Product.	Precipititate Formation. Reagent Number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Propadrin												*b*					
o-Hydroxy-propadrin					**b**												
m-Hydroxy-propadrin					*w*	*w*						*b*					
p-Hydroxy-propadrin					b							b					
m-Hydroxy, *p*-methylpropadrin												b					
p-Hydroxy, *m*-methylpropadrin					*y*		*b*	*y*				b		*w*			
m, *p*-Dihydroxy-propadrin (nor-homo-epinephrine)					*Y*												
Epinephrine					*B*												

TABLE III.—PHENOLIC DERIVATIVES.

Product.	Color Reaction. Reagent Number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Propadrin																	
o-Hydroxy-propadrin		y			Y				p								
m-Hydroxy-propadrin			y						*p*b								
p-Hydroxy-propadrin		*Y*			*Y*				*p*			B					
m-Hydroxy, *p*-methylpropadrin		y							*bl*								
p-Hydroxy, *m*-methylpropadrin		y			*Y*				*bl*								
m, *p*-Dihydroxy-propadrin		bY			**Y**				*G*	*R*		R			*R*		*Y*
Epinephrine		b*Y*			**B**				g	*R*		RB					r*Y*

TABLE IV.—METHYL ETHERS.

Product.	Precipitate Reactions. Reagent Number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
o-Methoxy-propadrin					w		*rb*										
p-Methoxy-propadrin		w															
o, *p*-Dimethoxy-propadrin					**w**		*b*	*w*				*b*					

TABLE V.—METHYL ETHERS.

Product.	Color Reactions. Reagent Number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
o-Methoxy-propadrin			*p*														
p-Methoxy-propadrin																	
o, *p*-Dimethoxy-propadrin		g	y	p								B					Y

TABLE VI.—AMINO-ALCOHOLS AND CORRESPONDING KETONES.

Product.	Precipitate Formations. Reagent Number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Propadrin												*b*					
Propadrone					*yw*	*w*						*b*					
o-Methyl-propadrone							*b*	*y*				*b*		*w*		*w*	
m-Hydroxy-propadrin					*w*	*w*						*b*					
m-Hydroxy-propadrone						*w*						*b*					
m-Hydroxy, *p*-methylpropadrin												b					
m-Hydroxy, *p*-methylpropadrone												*b*					*w*

TABLE VII.—AMINO-ALCOHOLS AND CORRESPONDING KETONES.

Product.	Color Reaction. Reagent Number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
m-Hydroxy-propadrin		*y*	y						*p*b								
m-Hydroxy-propadrone		*y*	*y*						*p*b								
m-Hydroxy, *p*-methylpropadrin		y							*bl*								
m-Hydroxy-*p*-methylpropadrone		y							*p*								

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THE LOCAL REACTIONS PRODUCED BY INTRAMUSCULAR INJECTION OF SOME ANTIMONY COMPOUNDS.*

BY A. E. JURIST AND W. G. CHRISTIANSEN.

Very little information is available concerning the physiological behavior of colloidal metallic antimony, sodium antimony iodide or antimony quinine iodide. In view of the fact that a number of antimony compounds such as tartrates, substituted phenylstibinic acids, derivatives of polyhydroxyphenols and of thioglycollic acid are either essential or of great value in the treatment of kala-azar, bilharziasis, leishmanioses and other protozoal infections, it appeared worth while to determine whether or not a colloidal antimony aqueous solution and sodium antimony iodide or antimony quinine iodide in ethylene glycol solution could be safely used in therapy. Knowledge regarding the biological behavior of these antimonials is also desirable for comparison with the behavior of analogous bismuth compounds. Solutions of these three substances were injected intramuscularly into

* Scientific Section, A. PH. A., Miami meeting, 1931.

dogs and particular attention was paid to the local reactions which developed. Also the toxicity and absorption of colloidal metallic antimony was studied. The nature of these preparations and the results obtained with them are described here.

COLLOIDAL METALLIC ANTIMONY.

The colloidal metallic antimony was prepared by a method which is essentially the same as that described by Gutbier and Kräutle (1), Usher (2), Gutbier, Ottenstein, and Allam (3) and Fouard (4). A completely reversible colloid containing 7.73% of metallic antimony was obtained. This was made up in aqueous solutions containing 15.5 mg. of antimony per cc., 7.7 mg. of antimony per cc. and 3.9 mg. of antimony per cc., respectively. The solutions were injected intramuscularly into dogs to observe the local reactions produced and into rats to determine the rate of absorption and toxicity.

Five intramuscular injections in four dogs produced marked swelling at the site of injection followed by a generalized swelling throughout the leg injected and finally abscess formation. The muscles were congested and hemmorrhagic and the animals suffered considerable pain. The reactions were very severe in every instance. When injected intramuscularly into rats the local reactions were again severe but absorption appeared to be complete within 48 hours. The dose required to kill 50% of the injected rats was 20 mg. of antimony per kilo. When injected intramuscularly and 16.5 mg. per Kg. when injected intravenously. The toxicity was about twice that of sodium antimonyl tartrate and the local reactions produced were too severe for a compound useful in therapy.

ANTIMONY IODIDE.

The preparation of antimony iodide is described by a number of investigators which are referred to by Mellor (5) so that they will not be mentioned individually here. Antimony iodide was prepared for this investigation by the following process. A saturated solution of antimony trichloride was prepared in ethyl acetate. This solution was then treated with an excess of sodium iodide added in small portions, shaking the solution vigorously after each addition of sodium iodide. The mixture was then filtered to remove excess sodium iodide and sodium chloride. The clear red solution containing the antimony compound was evaporated to dryness *in vacuo* over sulphuric acid. The dry power obtained contained 27.5% of antimony compared to a theoretical antimony content of 23.94% for SbI_3 due to the presence of some antimony oxyiodide. A solution of this compound in ethylene glycol was prepared using 5 Gm. of antimony iodide and 10 Gm. of sodium iodide in 50 cc. of ethylene glycol. Each cubic centimeter of solution contained 25.7 mg. of antimony per cc. The clear red solution so obtained was injected intramuscularly into dogs.

Two intramuscular injections of $^1/_2$ cc. each of this solution diluted with an equal volume of ethylene glycol, a total of 12.8 mg. of antimony for each injection, were given to each of two dogs. The local reactions were most severe. There was local sensitiveness and considerable pain followed by a local lump formation at the site of the injection and great swelling of the lower part of the leg. Finally an abscess formed with a punched out ulcer and drainage of a hemmorrhagic exudate. Control injections of ethylene glycol produced no local reactions whatever so that the severity of the local reactions obtained with this antimony compound were due

solely to the antimony compound and not to the solvent. The results demonstrate clearly that the compound is unsuitable as a therapeutic agent.

ANTIMONY QUININE IODIDE.

Antimony quinine iodide was prepared in a manner similar to that described by many investigators for bismuth quinine iodide, 4.5 Gm. of antimony trichloride were dissolved in 600 cc. of water and 200 cc. of concentrated hydrochloric acid. This solution was then added to a solution of 30 Gm. of sodium iodide and 6 Gm. of quinine hydrochloride in 600 cc. of water. A yellow precipitate was formed which was collected on a Buchner funnel, thoroughly washed with water, and then dried *in vacuo* over phosphoric anhydride. The dry powder contained 9.75% of antimony. A solution of this compound in ethylene glycol was prepared by dissolving 10 Gm. of compound and 20 Gm. of sodium iodide as a stabilizer in 100 cc. of ethylene glycol. The resulting clear red solution contained 11.6 mg. of antimony per cc. The results of intramuscular injection of this solution are as follows:

A single injection of 1 cc. of this solution was made in each of two dogs. The results were similar to those obtained with sodium antimony iodide. The injections cause marked local sensitiveness and considerable pain. This was followed by local lump formation, and tremendous swelling with extension through the injected leg. Subsequently there was abscess formation and a punched out ulcer as before. The reactions were as severe as in the case of sodium antimony iodide and show that this compound, too, is useless as a therapeutic agent.

The severe local reactions produced by all three compounds described here are sufficient evidence that they are not safe therapeutic agents. This is directly opposite to the results which have been obtained with analogous bismuth compounds. Bismuth quinine iodide has long been used in oil suspension or aqueous suspension in syphilis therapy without severe local reactions and bismuth metal in finely divided aqueous suspension or as a colloid does not cause local reactions. In similar studies with ethylene glycol solutions of bismuth iodide complexes local reactions were absent. The great difference between the antimony and bismuth compounds is surprising in view of the great chemical similarity of these two elements which are closely related in the same group of the periodic system. The results show clearly the impossibility of drawing conclusions regarding the most satisfactory means of administering a metal in therapy from results obtained with another metal no matter how closely the two may be related chemically.

The authors wish to acknowledge their appreciation to Mr. H. A. Holaday and his collaborators for carrying out the animal tests in the Biological Research Laboratories of E. R. Squibb and Sons.

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RESEARCH DEPARTMENT OF THE CHEMICAL AND PHARMACEUTICAL LABORATORIES,
E. R. SQUIBB AND SONS, BROOKLYN, N. Y.

A NOTE ON THE ASSAY OF TINCTURE OF FERRIC CHLORIDE.*

BY MARGARETHE OAKLEY AND JOHN C. KRANTZ, JR.

INTRODUCTION.

The tenth revision of the United States Pharmacopœia directs Tincture of Ferric Chloride to be assayed iodimetrically. This assay has been official for three decades. It was criticized by G. S. Ferrey (1) "on the grounds of inconvenience and large experimental error." In a study of the iron determinations for the eleventh revision of the Pharmacopœia the authors found the criticism of Ferrey to be warranted. The official method requires a weighed charge of the tincture to be employed. This seems unnecessary as the specific gravity of the tincture is approximately unity, and furthermore it is prepared upon a volume to volume basis. A portion of the tincture is evaporated to dryness, presumably to remove the alcohol, which appears to be an unnecessary procedure, as a preliminary step in the assay. The residue is dissolved in hydrochloric acid and hydrogen peroxide solution added presumably to oxidize any ferrous salt present to the ferric state. This step seems unwarranted as the solution from which the tincture is made is required to be free from divalent iron and the tincture is required to be preserved in amber-colored bottles protected from the light. The official definition, which standardizes the product in terms of trivalent iron is frustrated to some extent by the assay. If the product is exposed to light and reduction to divalent iron ensues, before titration the official assay insures that this is converted into the trivalent state and determined as such.

Furthermore in the official assay the reaction mixture is set aside for 30 minutes at 40° C. before titration. E. H. Swift (2) very recently made a critical study of this method of estimating the ferric ion. This investigator concluded that when the reaction between the ferric chloride and the iodide is allowed to take place in a closed flask for a period of only 5 minutes at room temperature a high degree of accuracy can be obtained. It was concluded also that the volume of the solution should be limited to 30 cc., 3 Gm. of potassium iodide should be present and from 0.25 to 25 milli-equivalents of hydrochloric acid.

With these facts before us the authors proceeded to modify the official assay method and study the relative accuracies of the procedures.

EXPERIMENTAL.

A series of 18 commercial samples of Tincture Ferric Chloride was examined. Each showed slight traces of ferrous iron. These were assayed by the official method using 5 cc.; and also by allowing the reaction mixture to stand and discharging the blue color, which re-appears owing to an insufficient quantity of potassium iodide, by adding more tenth-normal sodium thiosulphate solution. These tinctures were assayed also by the following modified procedure.

Pipette 5 cc. of the tincture into a suitable flask. Add about 20 cc. of distilled water, 3 Gm. of potassium iodide, and 3 cc. of hydrochloric acid. Titrate the iodine with tenth-normal sodium thiosulphate solution using starch T.S. as an indicator if preferred by the operator.

Table I shows the results obtained by the three methods.

* Scientific Section, Miami meeting, 1931.

TABLE I.

No.	U. S. P. First End-Point, Per Cent Fe.	U. S. P. Second End-Point, Per Cent Fe.	Modified Method, Per Cent Fe.	No.	U. S. P. First End-Point, Per Cent Fe.	U. S. P. Second End-Point, Per Cent Fe.	Modified Method, Per Cent Fe.
1	4.83	4.99	5.04	11	4.42	4.89	4.78
2	5.29	5.39	5.47	12	4.67	4.80	4.85
3	4.74	Lost	4.86	13	4.65	4.73	4.77
4	6.73	6.77	6.76	14	4.14	4.76	4.83
5	4.33	4.41	4.39	15	4.56	4.64	4.69
6	4.58	4.61	4.67	16	4.50	4.55	4.62
7	4.36	4.39	4.52	17	4.15	4.36	4.48
8	5.32	5.38	5.72	18	4.68	4.85	4.96
9	4.64	4.73	4.77				
10	4.14	4.72	4.83	Mean	4.71	4.88	4.94

These results indicate that the present official method and the modified method correlate quite well, however, the mean of the modified method is higher than that of the official method or of the second end-point reading of the official method.

A sample of the tincture was assayed gravimetrically using 1 cc. The first determination yielded 91.1 mg. Fe_2O_3 corresponding to 6.37 per cent Fe; the second determination yielded 90.8 mg. Fe_2O_3 corresponding to 6.35 per cent Fe; the third determination yielded 92.5 mg. Fe_2O_3 corresponding to 6.46 per cent Fe; the fourth determination yielded 91.7 mg. Fe_2O_3 corresponding to 6.41 per cent Fe.

This sample was assayed several times using the official method and the modified method. The results obtained are recorded in Table II.

TABLE II.

No.	U. S. P. Per Cent Fe.	Modified Method, Per Cent Fe.	No.	U. S. P. Per Cent Fe.	Modified Method, Per Cent Fe.
1	5.91	6.14	10	6.05	6.12
2	5.99	6.14	11	5.84	6.08
3	5.85	6.08	12	5.82	6.15
4	5.88	6.15	13	5.97	6.15
5	5.94	6.12	14	6.03	6.08
6	5.91	6.08	15	5.98	6.12
7	5.89	6.08			
8	5.98	6.08	Mean	5.94	6.11
9	6.03	6.11			

The probable error of a single determination was calculated by the formula

$$r = \pm 0.6745 \frac{\Sigma (V^2)}{N - 1}$$

The probable error of the mean of the series determinations was calculated by the formula

$$R = \pm 0.6745 \frac{\Sigma (V^2)}{N (N - 1)}$$

In these formulas V is the deviation from the mean and N the number of determinations. For the U. S. P. method $r = \pm 0.054$ per cent and $R = \pm 0.014$ per cent. For the modified method $r = \pm 0.019$ per cent and $R = \pm 0.005$ per cent.

The modified method more closely approaches the percentage of iron obtained by the gravimetric method, and is more rapidly carried out. The probable error of the modified method is far less than that of the U. S. P. method.

The P.E. of a single determination by the modified method is about 0.02 per cent, *i. e.*, the chances are even that one in two determinations will be either mean ±P.E. or that it will differ from the mean by more than one P.E.

SUMMARY.

A statistical study of the data obtained on the assay of Tincture of Ferric Chloride shows the modified method described herein to be more accurate than the present official method. The method is more rapid and less cumbersome.

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BUREAU OF CHEMISTRY,
MARYLAND STATE DEPARTMENT OF HEALTH.

HARDENED GELATIN CAPSULES.

J. D. B. Hubers van Assenraad (*Pharm. Ztg.*, 77, 27, 371), states that a capsule more satisfactory than by keratin coating can be prepared by the following process: the capsules are closed by dipping them into collodion. Into the bottom part of a desiccator a layer of cotton wool is spread and sprinkled with one cc. of formaldehyde solution for each liter of capacity; above this the capsules are placed on a piece of absorbent gauze, and allowed to remain from ten to twelve hours.

MEETING OF FEDERAL WHOLESALE DRUGGISTS ASSOCIATION.

The dates for the Convention of the Federal Wholesale Druggists Association have been changed to October 4th, 5th and 6th. This was done in order that the time of our Convention would not conflict with the Convention of the N. A. R. D. The City in which the Convention will be held is Washington, D. C., and the headquarters will be at the Hotel Raleigh.

ANTOINE BAUMÉ, FRENCH PHARMACIST.

Antoine Baumé, best known in connection with the hydrometer bearing his name, ranks high among the French pharmacists of the 18th century, who contributed largely to the chemistry of that period. He was born—February 26, 1728—at Senlis, about twenty-five miles distant from Paris, where his father was an inn-keeper. When thirteen years of age Antoine was apprenticed to a pharmacist of Compiegne, a town in which a royal palace of a previous century was rebuilt during the reign of Louis XV; the statement is incidental; however, his acquaintance in Compiegne may have given Baumé a hearing before the King, referred to hereafter.

In 1745 the young pharmacist came to Paris, where he found employment with Claude Joseph Geoffroy, the last of a lineage of pharmacists who had held this business from 1638 until 1762; the employer of Baumé was then about sixty years of age and highly regarded at home and abroad—he was a member of the Academy of Sciences and a fellow of the Royal Society of London; other members of this family were prominent among the scientists of that period. In the Geoffroy pharmacy Baumé served for six years, in charge of the laboratory. It was during this period that he made application to be received as a member of the Paris Guild of Apothecaries; objections were raised to his admission on account of deficient education and because he had not passed his apprenticeship in Paris. Baumé appealed to the King and, in 1752, was duly enrolled among the master apothecaries of Paris. It was in this year that Geoffroy died, and Baumé opened a shop in the rue St. Denis, opposite the Church of Saint Leu, having been aided financially by Joseph Macquer, Master of Pharmacy and Doctor of Medicine, known for a number of notable chemical discoveries and as director of the royal porcelain factory at Sevres; potassium arsenate was for a long time known as "Macquer's arsenical salt"—"Sal arsenicale Macquer." In 1763, the business which Baumé had founded was removed to rue Coquilliere where a wholesale as well as retail business was carried on.

Baumé disposed of his business interests in 1784, but in later years he suffered financial reverses and reëntered business as a partner of his son-in-law, Louis Margueron, a military pharmacist who, in 1800, opened a retail pharmacy, not far from Baumé's first shop; this partnership continued until the death of the latter, October 15, 1804.

During the more active years of his business life Baumé established a factory for the manufacture of sal ammoniac and devised a process of bleaching silk. He is, perhaps, best known, as previously stated, in connection with the areometer which bears his name; however, as pharmacist he deserves an honored place in pharmaceutical history for his successful efforts in removing many of the traditional superstitions which for a period burdened and afflicted the materia medica with polypharmacal combinations of disgusting ingredients. Baumé contributed largely to the new nomenclature of chemistry proposed by De Morveau, Lavosier, Bertholet and Fourcroy. Pharmacy claims Baumé as a pharmacist, he always searched for truth, this and his industry characterized him.

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All articles in these lists will be presented in abstract form in the bound volumes of the Year Book, which is issued annually. Those desiring abstracts immediately can obtain them for a fee of one dollar each by communicating with A. G. DuMez, University of Maryland, School of Pharmacy, N. W. cor. Lombard and Greene Sts., Baltimore, Maryland.

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CASTILE SOAP DECISION.

The U. S. Circuit Court of Appeals for the 7th circuit has rendered a decision which reverses the order of the Federal Trade Commission requiring that manufacturers seize and desist from the use of the term castile soap to designate soap made from fats other than olive oil. This is the Kirk case which has long been binding. The Court said in part:

"The government, through its agency the Bureau of Standards, has thus committed itself to the proposition that castile soap may be made of oily and fatty elements other than olive oil. Being solely a question of fact we deem it expedient for other departments of the government, including the judiciary, to accept such construction, if for no other reason than that of consistency."

DEPARTMENT OF BUSINESS MANAGEMENT

Conducted by Paul C. Olsen.*

COMMENTS, QUESTIONS AND SUGGESTIONS ARE INVITED AND WELCOME.

Readers are invited to submit comments, criticisms and suggestions regarding the material which appears in this department. The Editor will also undertake to answer questions regarding general problems of business management. Letters of general interest will be published, but the writer's name will not be revealed without his permission.

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ADVERTISING AND SELLING PROBLEMS OF DRUG STORES.

HOW TO WRITE EFFECTIVE BUSINESS LETTERS.

BY PAUL C. OLSEN.

Every letter written or received by a retail druggist is really a sales letter. When a druggist writes a letter, he writes it, or he should write it, with the purpose in mind of impressing a definite feeling or action upon the person who receives the letter.

In just the degree to which a letter is successful in doing this, the sender is successful as a letter writer.

Business letters are written by pharmacists for the following purposes:

1. To sell goods and services.
2. To make an inquiry.
3. To reply to an inquiry.
4. To give instructions.
5. To order goods.
6. To make acknowledgment.
7. To ask for credit.
8. To collect bills.
9. To adjust complaints.
10. To make introductions, endorsements and recommendations.
11. To apply for a position.

Because a pharmacist is likely to have to write letters of these various kinds throughout his career, it is of the utmost importance and profit to him that he should understand and be able to apply the factors which obtained for business letters maximum effectiveness.

These factors which obtain maximum effectiveness for business letters are four in number.

The first is, *appearance* and *form*. A letter which is not physically attractive is unnecessarily handicapped. Letters should have an appearance appropriate to their message. It is not necessary for a letter calling the attention of backyard gardeners to a drug store's stock of seeds to be written on stationery suitable for announcing social functions. Contrarily, a letter intended to attract more stationery sales to a drug store should not be smearily mineographed on a sleezy sheet of paper.

Time is the second factor affecting the success of business letters. A letter should reach its reader, when possible or determinable, at a time when the letter can get and hold the reader's maximum attention. Full advantage should be taken

* Lecturer on Business, Columbia University and Philadelphia College of Pharmacy and Science.

of environmental and competing influences to do this. It is wasteful to send letters in July about school supplies to parents of children of school age.

Time is a factor, however, which is decidedly individual in its force. Who would believe, for instance, that a druggist could sell Christmas cards by letter to his customers a few days after Christmas? There are druggists who do this year after year, incidentally disposing of left-over stock which they otherwise would have to carry until the following Christmas season. The money thus received from these extra after Christmas sales is thus available for the purchase and sale through the winter months of additional medicines and pharmaceutical necessities which are in greatest demand at that time of the year. The plan is logical. Greeting card manufacturers themselves send their own salesmen out to drug stores in January, selling Christmas cards for the following season and do so successfully because the memory of the preceding seasons' business is still fresh in the minds of their retail distributors.

The *English* used in letters written by retail druggists is a third factor influencing the effectiveness of these letters. Business letters should be written in a style which will convey the message to the reader most readily and effectively. This means that a business letter should be written simply, directly and clearly, and in a style not calculated to attract attention to itself to the detraction of the attention given to the message.

The comment, "Isn't this a clever letter I had from Galen's drug store this morning?"—is really a severe indictment of the effectiveness of that letter, although the recipient of course doesn't intend his comment to be taken that way. The message is the important thing about a letter, not the form in which it is conveyed. If the English and the form of a business letter are so unusual as to attract attention to themselves, there is just that much less likelihood of the message being understood and acted upon.

The words and expressions used in an effective business letter should be those which will be most readily understood and appreciated by the particular readers addressed. Oriental pidgin English may be uproariously entertaining to some people but it rarely helps readers to understand and act upon the message expressed in letters written in this style. The wording of a business letter should be a help and not a hindrance to the understanding of the message of the letter.

Fourth and most fundamental factor of all in the success of a business letter is the *message* itself. A business letter may be attractive in appearance and form, arrive at an appropriate time and be phrased in excellent English; yet if it conveys no message which arouses interest and a desire to respond, the letter is useless.

The ideas and thoughts in a business letter should be related to the experience and interests of the person addressed. Manufacturers and wholesalers when writing letters to retail druggists try to talk the language of retail pharmacy because they know that this will impress retail druggists with their familiarity with his situation and problems. When a retail druggist writes letters to the physicians practicing near him, he tries to talk the language of the physician so that the physician will be impressed with the pharmacist's understanding of the problems of his practice. Then the physician is more likely to call upon the pharmacist for professional services.

In writing to lay customers, the variety of their interests and environments

sometimes prohibits a message intimately associated with their individual problems. It is possible, of course, to write special letters to parents of young children, calling attention to the drug store's ability to serve them. When general letters are written the likelihood of their producing interest and a profitable response can be increased by appeals based upon local customs, traditions and habits and, more generally, upon the instincts and the emotions.

In many of the southern states, spring house cleaning begins traditionally the first week in April. Therefore, a druggist in the south who sends to the housewives in the vicinity of his store letters about house-cleaning aids in his stock the last week in March can be almost sure that a large proportion of the housewives who receive this letter will be interested in its subject matter. Special selling efforts at Easter time, Mother's Day and now in June, Father's Day, school opening, fall house cleaning, Hallowe'en, Thanksgiving and Christmas all rest upon the same fundamental basis.

Appeals in drug store sales letters to instincts are likely to be effective because instincts are an inherited and universal tendency people have to respond to similarly under similar conditions. No one knows yet how many instincts there are. The following list, however, enumerates some of the instincts toward which appeals in sales letters are commonly and effectively directed:

1. Appetite
2. Bargain (something for nothing)
3. Comfort
4. Family
5. Play
6. Self preservation
7. Acquisitiveness
8. Hunting
9. Sociability
10. Competition
11. Curiosity
12. Ornamentation
13. Cleanliness
14. Imitation
15. Construction
16. Harmony and beauty.

As is the case with instincts, psychologists do not yet know all of the characteristics of emotions. Emotions are mental states which may accompany instinctive actions or they may occur independently of them. Their importance as bases of appeal in sales letters is their inherited and universal occurrence in all people.

Emotions which occur frequently independently of instinctive action are the following: Joy, Sorrow, Sympathy, Humor and Restlessness.

Modification of instincts and emotions is believed now by psychologists to occur almost from birth. Civilization curbs the acquisitive instinct we all have; imperfectly, though, in many instances, otherwise there would be no need for police departments. Environmental modification of instincts naturally reduces the likelihood of response to appeals to these instincts. None the less, instinctive appeals can be tremendously effective. Given no knowledge at all about the individual tastes and inclinations of a person to whom a sales letter is to be addressed, isn't it more likely that a sales letter based upon an instinctive or emotional appeal will be more likely to be effective than one which is based upon an appeal which may not be within the experience or interest of the person addressed?

In sales letters, suggestions combined with a subordinate justification are the most effective bases for an appeal designed to secure immediate response. People do not like to think that in responding to a sales letter, they acted impulsively. Therefore, the wise sales letter writer also includes in his message, in addition to the

instinctive or emotional appeal subordinate reasons which, when the reader reflects upon his response, will provide him with a justification for that response.

Specifically, an appeal to a young mother in a sales letter to buy at a drug store strained vegetables for her infant may be based primarily upon the family love instinct. The letter should include in addition, however, a justification for the purchase, "Baby's health will be cared for. Care in infancy prevents many later ills."

Logical reasoning in sales letters is useful when action can be secured only after careful consideration. Generally it involves a choice of alternatives. Consider the problems involved in writing an effective letter which will convince a dispensing physician that he will serve his practice best and profit most if he writes prescriptions to be individually compounded by retail pharmacists rather than that he dispenses prepared medicines from his office.

Experienced druggists will see immediately in this and other like situations that logical reasoning should not be carried to the extreme of argument. Even when an argument is won, the reader of an argumentative sales letter feels that he has been forced unwillingly to an unwelcome conclusion. His attitude is one of grudging and crestfallen consent when it should be one of enthusiastic approval. The aim of every business letter should be to arouse a willing response.

BELLADONNA MONOGRAPHS.

BY FREDERICK B. KILMER.

(*Continued from page 375, April number, Jour. A. Ph. A.*)

DARIES' THESIS: "ATROPA BELLADONNA."

A notable landmark in the monographs devoted to Belladonna is one written by a Hamburg drug clerk, Peter John Andrew Daries, and published in 1776.

It was a graduation thesis submitted at the University of Leipzig, where he attained the degree of Doctor of Medicine.

This pamphlet monograph contains forty pages, and carries no illustrations. Not many copies are extant, and it is not generally referred to in the literature of the drug. The title page runs as follows:

"Concerning Atropa Belladonna
By The Authority Of The Most Gracious Order of Physicians
Under The Direction Of
Master Anthony William Plaz
Primarius Of Therapeutics, Dean Of The Medical
Faculty, Senior Member Of The National Saxon
Academy, Member Of The Board Of Governors, 'Greater Chief' Colleague Of
The College, Member Of The Academy Of Natural Curiosities.

The Author, Peter John Andrew Daries, Bachelor Of Medicine,
Of Parchimo-Metropolitanus,
Will Dispute For The Degree Of Doctor. On August 30, 1776."

Leipzig—From the Langenheim Printing Office.

The thesis is written in Latin. While it bears evidence of careful study and preparation, its actual putting-together seems to have been hastily performed. Citations of authorities are numerous, but mainly those of the century in which the thesis was written. He did not search the ancient or classical writers.

Daries summarizes his thesis as follows:

"I will first give the various names of belladonna, next the botanical characters, then the constituted principles and official preparations, then the salutary and toxic effects will be expounded, and I will adhere chiefly to the powers of the roots, leaves, berries and seeds, with the additions which are discovered after death by autopsy. Then I may add what I, myself, have observed, and last of all will speak concerning the antidotes of belladonna."

In Daries' time the plant had become *Atropa belladonna*. He gives a very complete nomenclature of the drug, with citation of authorities for its use. His description of the plant is from personal observation. A list of countries in which the plant has been found is given. The use of the juice of the plant as a wrinkle remover and beautifier by the Italian women is noted.

Daries had obtained from the plant, by distillation, aromatic products with a yellow, oily, waxy residue and fixed salts. These constituents do not account for the peculiar powers of the plant. Poisonous plants, according to Daries, act "chiefly by a meandering vaporosity." This principle "gravolent and vaporous, infects and contaminates the fluids of the brain and parts of the nerves, suppresses their powers and stops vital action."

The curdling action of the juice of Belladonna upon milk seemed to Daries to typify its action upon the fluids of the body. If expressed in modern terms, Daries' explanation would be found to concur in part with our knowledge of the physiological action of the drug.

A fertile field for historical study lies in the section on "official preparations" which exhibits the author's training in pharmacy. He enumerates a score of preparations in use in his time in which the herb, the berries, the juice and the root are used.

Daries asserts all parts of the Belladonna plant are poisonous. He attempts to show that the power and effects produced by the root, leaf and berries vary from each other. This belief is still held by some of our present-day writers.

With Daries, as with many others, the poisonous power of the berries "smiling to the eye, but with poison in every drop of their luscious juice" is recorded. He notes that Belladonna is shunned by certain animals and by others eaten with impunity.

A sidelight on pharmacology of the past is noted in instances where Belladonna is injected into the stomach of animals in order that its effect may be observed. It took many centuries up to Daries to reach the conclusion that the power, the varying symptoms, and the results depended upon the amount of the drug injected, and that the action of the drug is influenced by age, sex, constitution and condition of the patient, and that some persons are tolerant to the point of immunity.

In a section devoted to "salutary effects" Daries breaks away from tradition and becomes at once an apologist and champion of Belladonna as possessing "worthy powers both in internal and external use."

He states that his century had been called the "toxophilic."

"I have especially read that belladonna is a poison, from the use of which any physician, no matter who, may prudently abstain (Blackwell).

"Lewis rejoices that it was abrogated by all authority.

"Hahn has said 'the question to be put is whether it is granted to an honest physician to use poisons?'

"But despite this reputation, I cannot see why I may not write of the very active poison and medicine—belladonna. Nothing seems to stand in the way of this, and I may have the good fortune to say something new concerning the effects of the drug."

This was, for the time, most presumptuous and unorthodox. The candidate for a degree was held to the citation of authorities recognized by the faculty. The candidate's own opinions and conclusions were to be rigidly barred from discussion. We may wonder how the thesis came to pass the conservative faculty of Leipzig.

Daries most heroically relates "experiments undertaken," and recites his epoch-making story.

"When a novice in the Hamburg pharmacy of my uncle, Orthman, Dr. Reimer desired some extract of belladonna. The fresh herb, with its flowers and fruit, having been finely comminuted, the better to boil out and extract the tincture, a bit of herb or drop of berry juice unfortunately spattered into my right eye.

"Realising this, I attempted in vain to remove the foreign irritant from the eye with the finger. Hardly had three minutes of the hour elapsed, the irritant action having ceased meanwhile, when a mistiness arose before the eye, which increased little by little. After quarter of an hour, there was present total blindness without any pain, the other eye remaining intact."

He sought the counsel of Dr. Reimer, the prescriber of the drug, and by proper treatment in three weeks his eye "was restored to its pristine integrity."

Reimer informed him that it was known that the ingestion of Belladonna would produce mydriasis, but he was surprised to learn that the external application of the drug would produce this result.

The discussion of the matter with Dr. Reimer resulted in the suggestion that this peculiar power of Belladonna might induce a harmless and temporary paralysis in the operation for cataract.

Through this the Hamburg drug clerk was stimulated to conduct a series of experiments upon animals.

His methods and results entitle him to a front rank as a pioneer in pharmacodynamics.

Quaintly he recites:

"If a cat or owl is placed in an utterly dark place, no light of any kind, and no light to appear, it is nevertheless reflected from the eyes, as soon as ever so little light is admitted.

"The eyes of these animals, before others, have the singular property that not only is the pupil much wider than the freer iris, and nowhere coherent to the cornea, but even the finest are pleased and moreover carry more also of aqueous humor between the cornea and crystalline humor, more remote from the pupil, but nearer to the retina, while endowed with non-pigmented choroid, and an obscure but pale flavescent or cerulean one. The conjunctival tunic of this cat, moistened with the juices of belladonna by means of a feather, one hour having hardly elapsed, the uvea became dilated, much more the right than the left, so that the chink was more than tenfold larger, and indeed assumed a circular shape, when formerly this had been oblong. In the eyes, moreover, nothing was seen of disease or cloudiness. Left to itself, the cat staggered as if drunk from the beginning, but a little later it walked with its accustomed gait, its head hanging, and tried with its fore feet to remove the application from its eyes.

"After an interval of two hours the phenomenon wholly disappeared, and the narrow longitudinal chink was restored to both eyes.

"With this experiment repeated with the dry herb in the right eye and the juice of the berry in the left, in a little while the uvea was dilated to the former circle. On the following morning the dilation of the pupil had again vanished. Therefore, instituting this experiment for the third time, the same result was obtained, but with this difference, that twelve hours having elapsed the pupils remained immobile.

"From this fact the cat was subjected to the anatomist's knife of my impartial friends, the distinguished Hebenstreit and Gerischer.

"In the alimentary canal, in the chest, abdomen and brain, no alterations were found. But on investigating the eye, the uvea, quite toward the wall of the sclerotic to which the choroid adheres, was flaccid and at the same time retracted in such manner that the pupil was tenfold larger than is found in the normal cat. The aqueous humor was clear, the vitreous indeed thin, almost watery, but nevertheless was quite soft.

"Likewise Rossi writes, 'dogs, cocks, chickens and small birds are disturbed by no sign of inflammation nor by pain, when their eyes are touched with a feather wet with the juice.' With two of the birds, a swallow and a lark, this experiment was carried out in the prescribed manner, and it is testified that this agrees perfectly with the truth, for the two birds developed no symptoms, the juice applied being gradually absorbed by the lacrymal points.

"These opinions, compared with the judgment of Dr. Reimer, concerning the application of belladonna as bound to induce a harmless temporary paralysis of the eye in order that extraction of the lens may be more readily carried out, seem to me to agree excellently."

Daries hastily concludes his monograph with this paragraph:

"Finished, therefore, is the copious discussion concerning the powers of belladonna, the salutary as well as the poisonous, which although possibly too lightly composed for a polished disputation, I submit to the judgment of the World of Letters."

We may well pause to pay due honor to this Hamburg drug clerk, Daries. His graduation thesis, now a "scrap of paper," adds much to the story of Belladonna. In it a condemned and rejected drug is restored to its rightful place in materia medica. What a loss to medicine and to mankind would have accrued if Belladonna and its narcotic congeners had remained under the ban which prevailed before Daries wrote his pamphlet. More than all, Daries opened the door which gave to the world a knowledge of the mydriatic action of Belladonna and other drugs of its class, a knowledge which conferred untold blessings upon mankind.

The world of letters, of medicine and of pharmacy—humanity itself—may well join in tribute to Peter John Andrew Daries.

BELLADONNA AFTER THE MONOGRAPHS.

The century following Daries, the last of the monographists, witnessed what might be termed a revolution in therapeutic practice, most notably the oncoming of organo-therapy, a sort of rebirth of the ancient animal therapy—physiotherapy—which was astrological medicine revamped.

In respect to the administration of drugs, many far-reaching changes occurred. A sceptical attitude arose in respect to the use of drugs in any form—a therapeutic nihilism and pessimism—and there was a strong battle against polypharmacy, which had prevailed in the previous centuries. The rise of homeopathy was a contributing factor in reducing dosage. Out of the conflict came a school which sought to study rationally and scientifically the action of drugs, old and new. In this turmoil, the solanaceous drugs, particularly Belladonna, have not only held their place, but advanced to new measures of usefulness.

More than forty years after Daries, another drug clerk, Runge (1810), had a similar experience to that of Daries in spattering the juice of Belladonna in his eye.

It started a train of thought that led to important results in the study of the mydriatic action of Belladonna and allied Solanums.

Runge, who is noted for his researches in the anilines, in consultation with the famous poet and scientist, Goethe, established the mydriatic action of other members of the solanaceous group. He separated what proved to be a mixture of the alkaloidal principles. This he called "Koromegen" (Greek—magnifier of the pupil). True Atropine was isolated in 1830 by the apothecary Mein; again independently in 1832 by Geiger and Hesse. Later, Leibig determined the chemical formula.

In the century following Sickels and Daries, we reach the time of multiplying literature. Belladonna and the mydriatic Solanums are treated systematically in books on materia medica, pharmacy, pharmacognosy and chemistry.

In the ever-increasing number of journals a mere list of titles of articles on these drugs, appearing in the period, would make up a portentous volume. An interesting feature of the medical literature lies in the vast amount of repetition. Many dissertations are found wherein the authors claim as a "discovery" of their own an action and use that had been noted hundreds of years before. Time and time again, writers issue a warning as to a "newly discovered" poisonous action of various parts of the Belladonna plant, the existence of which had been known for centuries. Extended, and at times acrimonious, has been the discussion as to the difference in action between the members of the related mydriatic plants and the various parts of the same plant. Hyoscyamus, Stramonium, Scopola and Belladonna have each had their advocates. The leaf, the herb and the root of Belladonna have been made official, and in turn deleted. Except in historical literature, the Mandrake has disappeared.

Full attention has been given to the use of the alkaloids in place of preparations from the plant, and likewise the shades of difference in the action of the different alkaloidal bodies. The methods of pharmacology have done much in the direction of clarification and simplification of the action of drugs, but in respect to Belladonna and like agents, the final test is at the bedside.

It was in the Nineteenth Century that real chemical methods were applied in the examination of Belladonna. In the first decade of the century, Louis Nicholas Vauquelin, an apothecary and director of the School of Pharmacy at Paris, is credited with the first proximate analysis. During the years that followed, a rather formidable list of substances have been laid down as having been found in Belladonna. Here are some of them:

Starch, sugars, honey and saccharates, cellulose, gums, wax, resins, mucilages, asparagine, albumin.

Coloring Matters: Chlorophyl, anthocyanin purple, xanthophyll yellow, atrosin.

Alkaloids: Atropine, hyoscyamine, belladonine, atropamine, apatropine.

Acids: Acetic, malic, chrysatropic, succinic, prendatorin, phyteumscolla.

Salts: Potassium sulphate, nitrate, phosphate, chloride, hydrochlorate, oxalate, malate; magnesium malate, phosphate; sodium chloride, phosphate; calcium malate, oxalate; ammonium salts.

Odoriferous and aromatic principles.

We cannot presume that all of the substances named in this array exist as such in Belladonna. Some of them no doubt are formed during the chemical manipulations

of the drug. But as they stand, they constitute our chemical knowledge of Belladonna, gained during the years following the monographs up to now.

In the pharmacy of the mydriatic group, much has been done upon processes of assay, upon the pharmacognosy, upon standardizing the actions of the drugs and upon methods of extraction. Except for the preparations of the alkaloids, pharmaceutical compounds have not changed materially since the time of the monographs. Notable is the fact that alcoholic extractions and preparations from fresh juice—the green extracts of the Continent—have persisted. Writers have repeatedly urged the need for improvement in the preparations of the mydriatic, as well as other vegetable drugs.

The cultivation of drug plants, including those in the mydriatic group, runs through all centuries. In the period following the one we are reviewing, advanced cultivation methods were applied to Belladonna, Hyoscyamus and Stramonium. This was stimulated by the increased use of the drugs, which caused a shortage of supply. The literature is filled with discussions as to the respective medicinal value of the wild and the cultivated drug. In the cultivation of Belladonna and Hyoscyamus, difficulties, which have not yet been mastered, were encountered, since these particular plants were greatly influenced by any change in their environment. As in previous centuries, the main source of supply for the mydriatic drugs in all countries remains in the hands of herb gatherers. This in itself prevents uniformity in methods of gathering and in conservation, and hence a variation in quality.

The literature of the Nineteenth Century is filled with discussions of pharmacopœial and legal standards and regulations for the control of the quality of Belladonna and the mydriatic Solanums. Nature has her own standards, which man cannot change. Neither pharmacopœias nor market regulations can control peasant gatherers in the mountain fastnesses. When the pharmacopœias based the standard of pharmacopœial preparations of the mydriatic drugs upon the alkaloidal content, commerce fixed the value of the drug upon a like basis. This was a sane and progressive step toward uniformity.

Notable in the Nineteenth Century was the growth of scientific medicine, the revival and extension of experimental investigation, the establishment of research laboratories—physiological, pharmacological, biological and chemical; the growth of specialism, advancement of diagnosis, the progress in medical education; the rise of preventive medicine on the foundations of bacteriology. The century includes the discovery of anæsthesia, Roentgen-rays and the entrance of surgery into the "Modern Era."

Osler tersely summarizes the Nineteenth Century as a period wherein

> "Science emptied upon man from the horn of *Almalthea* blessings which cannot be enumerated, blessings which have made the century forever memorable, and which have followed each other with a rapidity so bewildering that we know not what to expect next. The great boon of this wonderful century, with which no other can be compared, has been the fact that the leaves of the tree of science have been used for the healing of the nations. This is the Promethean gift of the century to man."

Through the revolutions and kaleidoscopic changes in medical practice, Belladonna and its congeners have retained their place in therapy. The separation of the alkaloids, to a degree, changed the form of administration and increased

the use of these drugs. At the end of the first quarter of the Twentieth Century, a writer (Sajous) frankly states that the many therapeutic properties that had been credited to Belladonna have been sustained by modern research. It holds a more exalted position than ever before in the history of medicine. In part, this has been due to the growth of scientific pharmacology, and in another part to the achievement of discovering the "vital principles" of the ancients—the alkaloids of modern pharmacy.

The three monographs here outlined consist of a few "leaves" from the history of Belladonna, covering, in part, two centuries and carrying it toward the opening of the Nineteenth. Each of the writers made material additions to the knowledge of Belladonna. Faber classified and systematized the records which had been put down and added his own far-reaching observations. Sickels gave a view of the drug as it appeared in his own age. Daries, through original research, opened the door which led to the production of the alkaloidal principles which have proven of such great value to mankind. To these three writers we may well accord due honor.

A modern writer has stated that "in respect to Belladonna, much has been written, much forgotten, but about it really little is known." What the future may have in store cannot be foretold. There is nothing to indicate that the usefulness of Belladonna and allied drugs will not continue. More than ever before, their place is firmly fixed among the most important drugs in our materia medica, and they are well worthy of the studious labor that has been bestowed upon them.

THE NEW MEDICINAL PLANT AND VOLATILE OIL PRODUCTION LABORATORY OF THE DIVISION OF DRUG AND RELATED PLANTS, U. S. DEPARTMENT OF AGRICULTURE.

BY A. F. SIEVERS.

The Division of Drug and Related Plants of the Bureau of Plant Industry, U. S. Department of Agriculture, has for many years conducted investigations on the production of plants yielding medicinal products and volatile and fixed oils at the Department's experiment farm near Rosslyn, Va., across the river from Washington, D. C. The main objective of these investigations has been to determine the cultural requirements of such plants and to study the quantity and quality of their products, with special consideration to the possibilities of such plants as commercial crops in this country. In the prosecution of this work it is necessary to maintain a laboratory at the farm to handle the crops produced in connection with the field experiments, including the drying of seed and herb, the grinding of the herb, the distillation of the volatile oils, and various other operations that are usually associated with such investigations.

The organization of this work began in 1902, but it was not until 1907 that it was permanently located on the Department farm in approximately its present location. A lath structure for partial shade was provided and numerous species of medicinal interest were placed under cultivation. About six years later a permanent exhibition garden with 39 beds was laid out and this has been maintained without interruption up to the present time. In recent years an area of approximately two acres has been devoted to the cultural experiments. Some plants that show par-

ticular promise are grown in sufficient areas to give reasonably reliable indications regarding yields and to furnish ample material for study, while the majority of species are grown only in single rows or in the exhibition beds. Concerning the latter, continuous performance records have been kept, and with respect to many such species cultural observations over a period of three decades will soon be available.

When the work was located at the farm in 1907, laboratory space was provided in a new building consisting of a one story and basement frame structure. The

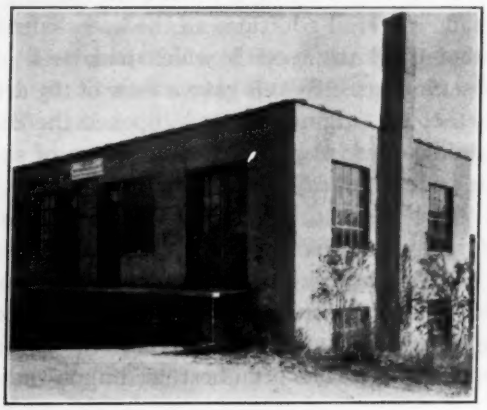


Fig. 1.—General view of the building.

Fig. 2.—Distilling room.

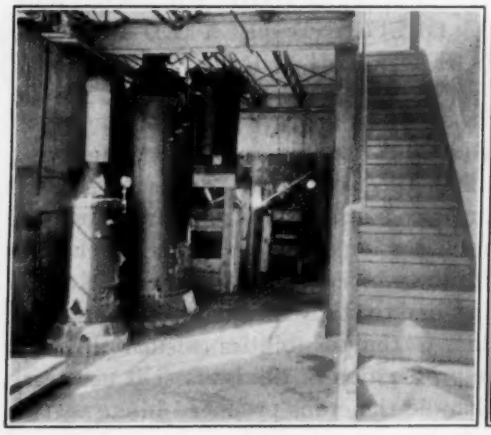


Fig. 3.—Boiler room.

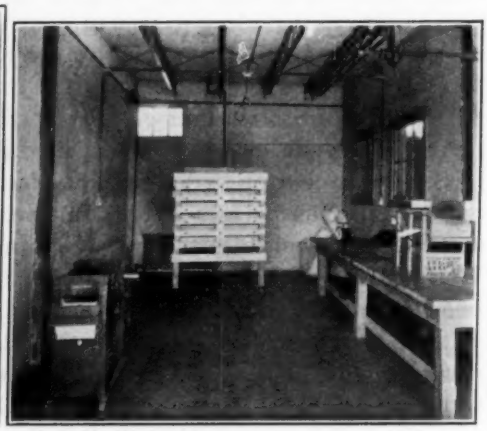


Fig. 4.—General drying and seed cleaning room.

nature of its construction made it a haven for rats, and made it impossible to keep the laboratory quarters clean. Under such conditions the work was carried on until 1930, when the entire building with its contents was destroyed by fire. On the same site there has been erected a new, modern, fireproof building, designed to meet the particular requirements of the work. The Division of Drug and Related Plants occupies approximately one-half of this building, the remainder being used for general farm purposes. Practically all new equipment has been installed, such

as grinding mills, volatile oil stills, etc., and many new features have been provided. The completion of this new and attractive workshop marks the twenty-fifth anniversary of the establishment of this line of work at the farm. It is entirely fitting, therefore, that a brief description of it by word and picture be given.

The building is constructed of poured concrete with cement floors, metal window frames and steel ceiling and floor joists. It is built on a side hill which permits convenient entrance to the main floor from one side and provides a ground level entrance to the basement from the opposite side, as indicated in Fig. 1. The small door shown at the left leads into a general storeroom, while that on the right is the entrance to the office. At the rear of the office is a small room with shelves and cabinets for storing the seed supply. The end room on the same floor adjoining the office on the right is the distilling room (Fig. 2). Double sliding doors and a loading platform at floor level make it convenient to deliver material for distillation and to remove the waste.

The distilling room is equipped with three stills. The large still in the front corner has a capacity of about 500 pounds of fresh herb. It is constructed of boiler plate and is mounted on a rack in the basement with the opening about a foot above the floor to facilitate charging and unloading. A chain hoist is used to lift the heavy top and to pull out the exhausted charge, usually in two batches. The two smaller stills are constructed of copper, tin-lined throughout, and connect with a vertical, tubular, copper condenser of which all parts coming in contact with the distillate are tin-lined. One of these stills is 18 × 28 inches with a capacity of 30 gallons, while the other is 22 × 40 inches and holds 65 gallons. Both are mounted on trunnions so that they can be tipped forward for discharging spent material into the small platform truck.

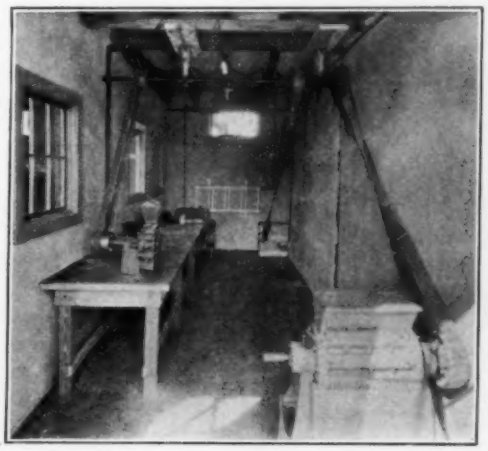


Fig. 5.—Mill room.

On the ground floor, below the distilling room, is the boiler room (Fig. 3). Two boilers, of 2 and 14 horsepower, are available for the operation of the stills. In the lower corner is shown a steam soil sterilizer, and in the rear is a hydraulic press used in connection with investigations on oil seeds.

Adjoining the boiler room on the right, and communicating with it, is a general workroom for various operations, such as drying herb, cleaning seed, etc. (Fig. 4). The movable rack holds six wire-bottomed drying trays. This rack can be pushed through double doors out into the yard for drying material in the sun if desired. The machine at the left is known as a dockage kicker. It is used extensively in grain elevators and has been found most useful for separating seed from chaff, especially seed of light weight that cannot be cleaned with a blower. A small fanning mill on the table is also used for cleaning seed. With these two machines on hand it has been found possible to clean satisfactorily practically all the types

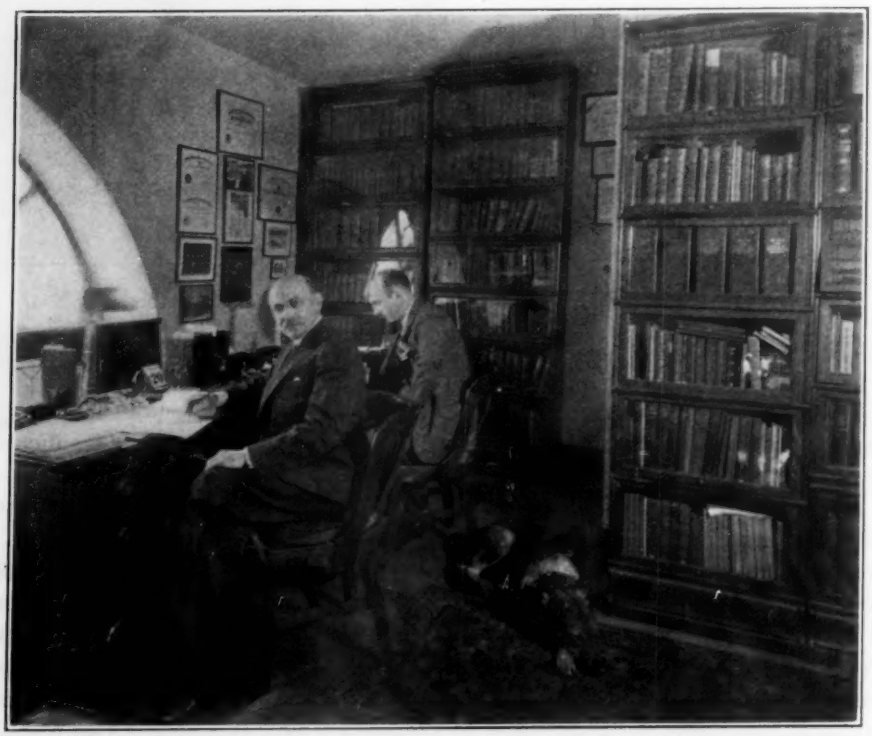
of seed produced in the experimental plots. It is planned to install a steam-heated dryer equipped with a blower at the rear of this room.

The mill room shown in Fig. 5 adjoins the room just described. Here all the grinding equipment is located. This consists of a powerful chopper or disintegrator at the right, a small mill for finer grinding at the left, and two pebble mills, a large one in the corner and a small two-jar type on the table. The pebble mills are driven by the small motor mounted on the bench in the adjoining room.

The general arrangement of the rooms and equipment has been found very satisfactory, although changes will no doubt be made from time to time and new ideas introduced to meet changing requirements. To those engaged in similar work the Division of Drug and Related Plants extends an invitation to visit this new laboratory.

Sir Henry Wellcome has favored us with Press reports of the Ceremony of the laying of the Corner Stone of the new Wellcome Research Institution on November 25, 1931. Also an illustrated booklet of the Ceremony and description of the various laboratories and museums which are housed in the new building, which will be completed by the end of this year.

Dr. Frederick B. Kilmer has favored us with a memorial booklet entitled "Annie Kilburn Kilmer"—extracted from newspaper notices. Mrs. Kilmer died January 1st of this year. She was the wife of our fellow-member and the mother of Joyce Kilmer, internationally known by the poem "Trees," for which the mother had composed the music.



Private office and part of library, Lascoff Pharmacy, New York City.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

"The following paper by Dean A. G. DuMez of the Maryland College of Pharmacy is very timely. Pharmaceutical education has been developing rapidly in the past ten years and a survey of its historical development in the United States is very beneficial to all pharmaceutical educators in determining whether we are on the right track or not. This very comprehensive paper by Dean DuMez gives an excellent survey. In addition, his references make it possible for us to look up the original material. I am sure that all teachers of pharmacy will find much of interest in the paper.—C. B. JORDAN, *Editor*."

DEVELOPMENT OF PHARMACEUTICAL EDUCATION IN THE UNITED STATES AND ITS PRESENT TREND.*

BY A. G. DUMEZ.

The practice of pharmacy as a separate or distinct profession in the United States may be said to have had its beginning in the years immediately following the Revolutionary War. While the records show that a number of so-called apothecary shops were established by persons other than medical practitioners[1] in earlier years and that in some few instances apothecaries educated in Europe[2] compounded medicines and dispensed prescriptions prior to that time, it is a well-established fact that practically all doctors of the colonial period carried stocks of drugs and filled their own prescriptions.[3] It was not until after the war that pharmacy as an inde-

* Paper presented before the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION, February 18, 1932.

[1] Otto Raubenheimer in an article entitled "Historical Sketches of Old Drug Stores in This Country" lists eight apothecary shops or drug stores established by non-medical practitioners in this country prior to 1780. These were located at Boston, New York, Perth Amboy, N. J., and Philadelphia. *Drug. Circ.* (October 1927), page 989.

[2] Mr. Leighton, an English apothecary, established himself in Philadelphia in 1765, where he advertised that he brought a large supply of medicines with him and that he was prepared to fill all prescriptions that should be presented to him. The outcome of this venture is not recorded. M. I. Wilbert, *Am. J. Pharm.*, 79 (1907), 402.

A shop was opened in Norfolk, Va., in 1772 by Robert Agnes, an apothecary from London. Blanton, "Medicine in Virginia in the Eighteenth Century," 1932, page 33.

The first appointment of an apothecary to fill prescriptions in this country other than his own was the appointment of Jonathan Roberts as apothecary to the Pennsylvania Hospital in December 1752. Benjamin Franklin, Account of the Pennsylvania Hospital from Its Rise to the Beginning of the Fifth Month, called May 1754.

[3] De Warville in writing of his travels in this country in 1788 says: "The greater part of these physicians are at the same time apothecaries. They continue to unite the two sciences, out of respect to the people, who wish that the man who orders the medicine should likewise prepare it." De Warville, "New Travels in the United States of America," performed in 1788, page 351.

In Baltimore, the compounding of prescriptions was mostly in the hands of physicians up to 1840. Prior to that time, the pharmacist was a mere vendor of crude drugs. "Annual Catalogue of the Maryland College of Pharmacy," 1891, page 9.

The conditions throughout Virginia were similar to those in Maryland. Such apothecary shops as were in existence before the end of the Revolution were owned and operated by physicians. Blanton, "Medicine in Virginia in the Eighteenth Century," 1932, pages 30–31.

pendent profession began to receive noteworthy support from American physicians.[1] The fact that the systematic education of young men to become its practitioners was not inaugurated until nearly half a century later is, therefore, not astounding. To trace for you the development of this field of education in our country from its beginning and to direct your attention to the present trend therein is the objective of this paper.

In the colonial days, the practice of pharmacy and medicine was carried on by one and the same person, usually a matron or a quack, frequently a clergyman and in the old established and more thickly populated settlements a physician.[2] But, as peace settled over the land following the War, agriculture, the trades and commerce grew apace and prospered and physicians educated and trained in Europe settled here in larger numbers. The more successful of these soon became so busily engaged with their medical practice that they had no time for the preparation of medicines and gradually relegated this work to those less successful or those especially interested in materia medica, to established dealers in drugs and medicines and to the apothecaries by education as they came here from Europe. In this way a differentiation between prescribers and dispensers gradually took place.

Dr. John Morgan was the first to publicly advocate the dissociation of the two professions.[3] On his return to Philadelphia in 1765 from Paris and Edinburg, where he had been studying medicine, he proclaimed the principle that physicians should confine themselves to prescribing, leaving to the apothecary the preparing and compounding of medicines. The first physician to have actually made a practice of writing prescriptions is said to have been Abraham Chauvet, who settled in Philadelphia in 1770. He was followed by John Jones, also of Philadelphia.[4]

It must not be inferred from the two cases cited that the principles enunciated by Dr. Morgan were generally accepted and that complete dissociation of the two callings took place immediately. As already stated, the process of separation was

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[1] Blanton attributes the change in the attitude of the physician to the influx of foreign doctors, "particularly those from Great Britain where the two branches had long been separated." "Medicine in Virginia in the Eighteenth Century," 1932, page 32.

[2] Of the early medical practitioners of the Massachusetts Colony, 6 or 7 (or more) were ministers as well as physicians; 1 was a doctor, schoolmaster and poet; 1 practiced medicine and kept a tavern; 1 was a butcher and 1 a female practitioner employed by her own sex. Lecture by Oliver Wendell Holmes delivered before the Lowell Institute, January 29, 1869.

The following description of the condition of medicine in the Colonies prior to the beginning of the Revolution is given in Smith's History of New York, page 326: "Few physicians amongst us are eminent for their skill. Quacks abound, and too many have recommended themselves to a full and profitable practice and subsistence. Any man at his pleasure sets up for physician, apothecary and chirurgeon."

Toner states that when the War of Independence began, and no American degrees existed, there were hardly more than 400 physicians holding European degrees in all the Colonies; and yet the medical practitioners numbered about 3500. Contributions to the Annals of Medical Progress, etc., 1874, page 106.

[3] Dr. Morgan in his "Discourse upon the Institution of Medical Schools in America" advocated "the regular mode of practicing physic" and recommended the complete separation of pharmacy and surgery from the practice of medicine. He wrote: "We must regret that the very different employment of physician, surgeon and apothecary should be promiscuously followed by one man; they certainly require different talents. Commencement address delivered at the College of Philadelphia, May 30, 1765. Printed by William Bradford.

[4] Blanton, "Medicine in Virginia in the Eighteenth Century," 1932, page 32.

a gradual one and it was many years before it was completed. The average medical practitioner was loathe to give up the additional fee he received for dispensing and the public did not take readily to the payment of two fees instead of one, one to the physician for treatment and one to the pharmacist for medicines.

This separation of the two professions, although definitely begun in the latter part of the eighteenth century, did not make much progress until the early part of the nineteenth century, when it appears to have become a part of a general forward movement which began about 1785 and which was characterized by a more marked specialization in the arts, trades and professions. Education, both elementary and higher, was improved and extended, and the standards of professional requirements and proficiency raised. Medical education advanced correspondingly and with the resulting increase in numbers and influence of a superior class of medical practitioners, a stricter discrimination in the arts of medicine and pharmacy gradually asserted itself. Some of the old-time general merchandise stores were converted into drug stores and dispensing apothecaries' shops; and these were conducted by men who grew up in the trade or men who were originally trained by physicians, and to a much smaller extent by pharmacists who immigrated from European countries.[1] This variety of pharmaceutical practitioners gradually amalgamated into one uniform profession with common aims and interests. One of these aims, the one with which this paper deals, was the inauguration of some system of education for their assistants commensurate with that already established for students of medicine. In the actual launching of this movement, however, the pharmacists were preceded by the medical men.

Pharmacy was already being taught in a number of the medical schools, but the courses were designed for medical students and were open to such students only. Martin I. Wilbert, in a paper on the beginnings of pharmacy in America published in 1907, wrote as follows regarding pharmaceutical education in the early medical schools: "The medical schools in different sections of the country early recognized the necessity of including instruction in pharmacy in their regular curriculum, and a number of them included pharmacy in the title of one of their professors. In 1820 no less than six of the twenty medical schools enumerated by Thacher in his 'History of Medicine in America' included more or less extensive instruction in pharmacy. The chair of pharmacy was usually combined with that of chemistry or materia medica, although in one instance it was combined with that of obstetrics."[2] This description of the status of pharmaceutical instruction in medical schools prior to 1820 is so comprehensive, in spite of its brevity, that the subject will not be pursued further except in one or two instances and these will be dealt with further on.

The first recorded attempt to teach pharmacy to others than students regularly matriculated in medical schools was made in the city of Philadelphia in 1816, by Dr. James Mease, a well-known medical practitioner and author. According to Dr. Joseph Carson, the historian of the Medical Department of the University of Pennsylvania, Dr. James Mease applied for and was granted permission to hold the introductory lecture to his course in pharmacy in the buildings of the Pennsylvania

[1] J. D. Schoepf, "Reise durch einige der mittleren und südlichen Vereinigten Staaten," etc., Erlangen, 1788, vol. I, page 121, through *Pharm. Review*, 16 (1898), 298.

[2] *Am. J. Pharm.*, 79 (1907), 406.

College.[1] Where, when and by whom the lectures were actually given is not known as the foregoing note made in the minute book of the Board of Trustees of the University of Pennsylvania is the only reference to the matter to be found.

The first provision for collegiate instruction in pharmacy in America was made by the first medical school to be established in this country, namely, the Medical School of the College of Philadelphia, which was opened in the City of Philadelphia in the fall of 1765, and which later became a department of the University of Pennsylvania. In the official announcement of the opening of the School it is stated: "In order to render the courses of lectures the more extensively useful, it is intended to introduce into them as much of the theory and practice of physic, of pharmacy and chemistry as can be conveniently admitted."[2] However, the chair of materia medica and pharmacy was not installed until 1789 and so far as I have been able to discover few if any pharmacists enrolled for the course.

The second attempt to supply the pharmacists' educational needs was also made by a Philadelphia institution, namely, the University of Pennsylvania. In 1819, the title of Professor of Materia Medica in the University was changed to that of Professor of Materia Medica and Pharmacy, and the lectures in these subjects along with those in chemistry were opened to students of pharmacy. The number of students who availed themselves of the privilege of attending these lectures appears to have been sufficiently large to have induced the officials of the University to take up the matter of making provision for a pharmacy degree. At a meeting of the trustees held on February 21, 1821, the following resolutions[3] were adopted on the recommendation and at the request of the Medical Faculty:

> "*Resolved*, (1) That the degree of Master of Pharmacy be, and is hereby instituted, to be conferred hereafter by the Trustees of this University on such persons exercising or intending to exercise the profession of an apothecary as are and shall be duly qualified to receive the same.
>
> "(2) That the faculty of medicine be requested to report to this Board at their next meeting a proper form of diploma and also a list of such apothecaries in the city and liberties of Philadelphia as are desirous and, in their opinion, deserving of the degree of Master of Pharmacy, and unless subsequent reasons to the contrary shall appear, the degree of Master of Pharmacy shall be conferred on such individuals, respectively.
>
> "(3) That every person who shall have served a regular apprenticeship of at least three years with a respectable apothecary or a master of pharmacy, and who shall exercise or intend to exercise the profession of an apothecary, in this State or elsewhere, may, on application to the Board, obtain the degree of Master of Pharmacy. Provided he shall produce a certificate of the faculty of medicine, signed by the Dean thereof, of his being qualified to receive the same, which certificate the faculty may grant on the attestation of the Professor of Chemistry and Materia Medica and Pharmacy, who shall have examined the candidate. He must also produce a certificate of his good moral character.
>
> "(4) That in future it shall be requisite for obtaining such a degree that the candidate shall have attended at least two courses of lectures on chemistry, materia medica and pharmacy in this University."

At the ensuing commencement, held on April 5, 1821, sixteen candidates re-

[1] Carson, "History of the Medical Department of the University of Pennsylvania," 1869, page 145.

[2] *Ibid.*, page 56.

[3] *Ibid.*, page 145.

ceived the degree of Master of Pharmacy. Unfortunately, this attempt on the part of an American University to recognize pharmacy as a branch of the healing art coördinate with medicine was checked by the pharmacists of Philadelphia, who believed that the physicians were endeavoring to control pharmaceutical practice, and the benefits of such a connection were lost to pharmacy for many years to come.[1]

The next step in this direction was taken by the practitioners of pharmacy themselves. On February 23, 1821, two days after the University of Pennsylvania had resolved to grant the degree of Master of Pharmacy, the apothecaries and druggists of the city and liberties of Philadelphia met in Carpenter's Hall to object to the step taken by the University and to organize themselves into a society "for the twofold purpose of providing a system of instruction in pharmacy, and subjecting themselves to regulations in their business." At subsequent meetings held on March 3 and 27, 1821, they organized the College of Apothecaries; and on March 30, 1822, their school was incorporated as the Philadelphia College of Pharmacy.[2] This school still functions to-day as the Philadelphia College of Pharmacy and Science.

The precedent set by the apothecaries of Philadelphia was followed by the pharmaceutical practitioners in most of the large cities of the country. The more important colleges of this type were established in Boston in 1823,[3] in New York in 1829, in Baltimore in 1841, in Chicago in 1859, in Cincinnati in 1870, in St. Louis in 1871, in Louisville in 1871, in San Francisco in 1872 and in Washington, D. C., in 1873. And, it must be admitted that the schools established by these colleges were well founded as all of them are still functioning as teaching institutions, although a majority have formed university connections and can no longer be considered as belonging to this group.

These schools founded and managed by pharmacists actively engaged in practice had for their primary objective the supplementing of the training received by apprentices in the drug stores and were operated mostly at night to suit the convenience of the employers. The nature of the instruction given by these institutions is perhaps best described in the words of Dr. Edward Kremers, Director of the Course in Pharmacy at the University of Wisconsin. At the fourth annual meeting of the American Conference of Pharmaceutical Faculties he spoke in part as follows: "The early history of all of these institutions clearly shows that they were 'Fortbildungsanstalten' closely affiliated with the daily routine of the drug store. The idea was not so much to give a thorough training in the fundamental sciences as to supplement the unsystematic training of the stores by a course of evening lectures. This truth is particularly emphasized by the fact that the clerk who had served an apprenticeship of two or more years attended the same course of evening lectures at least twice. It was the apprenticeship system improved but still essentially the apprenticeship system. The time spent in the store was, therefore, the

[1] Pharmaceutical education was not accorded equal recognition until 1876, when a school of pharmacy was established at the University of Michigan.

[2] "First Century of The Philadelphia College of Pharmacy," 1922, pages 65–68.

[3] The Boston College did not set up an organization for giving instruction in pharmacy until 1867. The school which was organized at that time is known as the Massachusetts College of Pharmacy.

prime requisite to a certificate of proficiency. The course of lectures simply served as a kind of superstructure, their prime object being to bring into some system the information and experience irregularly acquired during an apprenticeship and assistantship of four or more years."[1]

The first coördinate school of pharmacy operated as a university unit was established at the University of Michigan in 1876.[2] This event, important in itself, is of particular significance because it ushered in the application of university methods and standards to pharmaceutical education in this country and marks the beginning of the present trend in this field.

This change in the old order was vigorously opposed by the independent schools on the ground that the university teachers lacked drug store experience and that such experience was a primary requisite for the training of pharmacists. Whether it was because of this opposition or for some other reason, there were no further developments of the kind until 1883, when a school of pharmacy was established at the University of Wisconsin. From then on, the movement rapidly gathered momentum and within the following thirteen years no less than eleven such schools were established, *viz.:* at Purdue University, 1884; University of Iowa, 1885; University of Kansas, 1885; University of Ohio, 1885; Cornell University, 1887;[3] South Dakota Agricultural College, 1888; University of Minnesota, 1892; Alabama Polytechnic Institute, 1895; University of Washington, 1895; Washington Agricultural College, 1896; and University of North Carolina, 1896. At the present time, instruction in pharmacy is offered by most of our state universities, the notable exceptions being the universities of the New England States, New York and Pennsylvania.[4]

The advantages of the university school of pharmacy over the independent school were recognized immediately by those familar with conditions. Dr. Frederick Hoffmann of Berlin, Honorary President of the AMERICAN PHARMACEUTICAL ASSOCIATION, in an address prepared for the golden jubilee meeting of that Association held in Philadelphia in 1902, in commenting on this phase of the development of pharmaceutical education in this country, made the following significant statement: "It was a great advantage and conducive to superior results of the earlier university schools of pharmacy, equipped with a full faculty and ample laboratory and museum appointments, that they at once installed the pharmaceutical students in the general classes of the respective branches and required attendance at all the lectures and laboratory work."[5]

Whether the advantages singled out by Doctor Hoffmann were alone responsible for the rapid advance made by the university schools we do not know, but we do know that university ideals took root almost immediately, and by 1895 they were already so firmly implanted as to draw forth the following statement which

[1] "Proc. Am. Conf. Pharm. Faculties," 1903, page 5.

[2] The department of Pharmacy of Tulane University of Louisiana, established in 1834, is reported to be the oldest of the schools of pharmacy connected with a university, but it was not a school of pharmacy in the sense accepted at present. *Pharm. Era* (March 1912), 180.

[3] Discontinued in 1890.

[4] At present there are 67 schools and colleges of pharmacy in this country. Of this number, 33 are integral parts of state universities or municipally supported colleges, 21 are units with university applications and 13 are independent institutions of the proprietary type.

[5] PROC. A. PH. A., 50 (1902), 113.

appeared in the proceedings of the section on education and legislation of the AMERICAN PHARMACEUTICAL ASSOCIATION for that year: "Institutions that were founded by 'impractical' university teachers have proven their right to existence to such an extent that those who criticized them in former days, though still ostensibly maintaining their earlier ground, are in reality undermining their own foundation by silently accepting the ground of their supposed opponents."[1] These ideals have continued to take root and spread until to-day it may be said without fear of contradiction that the university schools now dominate in this field and that the trend in pharmaceutical education as a whole is distinctly toward the standards set by them.

The questions naturally arise: What are the standards set by these schools? What has caused the trend in pharmaceutical education to assume its present course? The statements immediately following are the answers in brief. The standards advocated by the university schools are those generally recognized in educational circles for work of collegiate grade. The placement of pharmaceutical education on an equality with that accepted as a standard by other university departments and their standardizing agencies is one of the chief aims of these schools. The reason for the drift toward the general adoption of these standards is that the body pharmaceutical of this country has finally awakened to the fact that, if the calling of pharmacy is to survive as a profession, the old idea of a course of study comprised almost wholly of subjects of strict pharmaceutical applicability and the employment of trade-school methods of instruction must be abandoned. The reorganization of the course of study to bring it into conformity with the broader curricula of other university departments and thereby give the student in pharmacy the same opportunity for independent study and research open to students of the other professions is a natural sequence. The extent to which we have progressed in this direction, as well as the nature of the progress made is depicted in a most interesting and striking way by the annual catalogues of the School of Pharmacy of the University of Maryland from which the following notes were taken.[2]

These catalogues, although intended primarily to convey information about the Maryland school, simulate so closely like publications of the other schools in nature and content that they serve to picture in a fairly accurate way conditions which were prevalent throughout the land. Taken as a whole, they, therefore, form a continuous record of the progress in pharmaceutical education made in this country during the last half century and leave no doubt as to its present trend. They record each step in the evolution of pharmaceutical education from the "Fortbildungsaustalten" stage to its present advanced state of development. They show that the requirements for admission were advanced about as rapidly as facilities for obtaining the required preliminary education became generally available, also the effect of the position taken by the American Association of Colleges of Pharmacy and the National Association of Boards of Pharmacy on this requirement as soon

[1] *Ibid.* (1895), 448.

[2] The annual catalogues of the School of Pharmacy of the University of Maryland, formerly the Maryland College of Pharmacy, are admirably suited to this purpose as the school began its existence in 1841 as an independent institution, became a part of the privately incorporated University of Maryland in 1904 and a department of the State University in 1920, when the old University of Maryland was merged with Maryland State College.

as these organizations became active, which was shortly after 1920; when the lectures were first graded so that second-year students did not merely repeat the work of the first year; when night courses were discontinued; when the recitation was first used as a method of instruction; the beginning and growth of laboratory instruction and how it gradually supplanted the apprenticeship requirement for graduation; each step in the broadening of the curriculum to meet new conditions or influences, and, particularly, in more recent years to bring it up to the standard set by the other professional schools; the times when the period of required attendance upon instruction was lengthened to meet the new conditions imposed by additions to the curriculum or for other reasons; the changes in scholastic standards; the evolution of the pharmaceutical degree and the changes in the requirements to be met by the candidates for degrees; and the stimulating effect of the mergence of the School with the University of Maryland in 1904 and the additional impetus given to advancement received when the School was made a department of the State University in 1920.

ANNUAL CATALOGUE AND ANNOUNCEMENT.

SCHOOL OF PHARMACY, UNIVERSITY OF MARYLAND.

(Maryland College of Pharmacy 1841–1904.)

Session of 1870–1871.

The prescribed course of study consisted of lectures in Pharmacy, Materia Medica and Chemistry.

Attendance upon two full courses of lectures given over a period of 2 sessions of about 18 weeks each was required for graduation. The candidate was also required to furnish proof of having served an apprenticeship of 4 years in the "drug and apothecary business" and to submit an original thesis of not less than 15 pages on some subject pertaining to pharmacy.

The degree conferred at graduation was Licentiate in Pharmacy. At the expiration of 3 years, upon evidence of professional advancement, the title of Master of Pharmacy was given; and upon those who maintained the honor and dignity of the profession for 10 years, the degree of Doctor of Pharmacy was conferred.

Session of 1871–1872.

Optional lectures on toxicology were offered.

The degree conferred upon graduation was changed from Licentiate in Pharmacy to Graduate in Pharmacy (Ph.G.).

Session of 1873–1874.

Laboratory work in Analytical Chemistry was required for the first time. This is the first instance in which laboratory work in chemistry was required by any of the schools of pharmacy of this country.

Session of 1878–1879.

The courses of lectures were graded to provide advanced instruction for the second-year students, or seniors. Previous to this time, the lectures were the same for all students, the seniors merely repeating attendance upon the lectures given in the first year.

Session of 1881–1882.

Attendance upon the lectures in Toxicology was made obligatory for graduation.

Session of 1883–1884.

A practical course in pharmaceutical manipulations was introduced. This is the first time laboratory work in pharmacy was offered.

Session of 1885–1886.

"Quiz Instruction" was introduced. Evidently, this was the first use made of the recitation as a means of instruction.

Session of 1886–1887.

With the beginning of this session, candidates for admission were required to pass a preliminary examination in "the ordinary branches of an English education taught in grammar schools; or to furnish in its stead a certificate of having passed an examination equivalent to that required for admission into the high schools of this city" (Baltimore).

Laboratory work in microscopy and practical botany was offered for the first time, but was not required for graduation.

Session of 1888–1889.

The length of a session was extended to cover a period of 6 months.

Laboratory work in the various branches of general chemistry was required for the first time.

Session of 1889–1890.

Beginning with this session, the time actually spent in attendance upon lectures and practical instruction in the chemical and pharmaceutical laboratories of the College was accepted as fulfilling in part the four-year apprenticeship requirement for graduation.

Session of 1891–1892.

The curriculum was divided into compulsory and optional studies, *viz.:*

Compulsory:	Pharmacy, Practical Pharmacy (Short Course), General Chemistry, Practical and Analytical Chemistry, Materia Medica, Botany and Pharmacognosy.
Optional:	Practical Pharmacy (Long Course), Microscopy, Practical Botany, Quiz Instruction.

Session of 1892–1893.

Beginning with this session, the lectures were given in the morning instead of in the late afternoon and evening.

The credit allowed for the time actually spent in practical instruction in the chemical and pharmaceutical laboratories of the College in the fulfillment of the four-year apprenticeship requirement for graduation was fixed at 6 months.

Session of 1894–1895.

Vegetable Histology and Pharmaceutical Assaying were added to the group of optional studies.

The practice of conferring the degrees of Master of Pharmacy (M.P.) and Doctor of Pharmacy (Phar.D.) upon graduates of the two-year course who had "maintained the honor and dignity of the profession" for 3- and 10-year periods, respectively, was discontinued at the end of this session. The total number of such degrees conferred was 21. Of these, 6 were Master of Pharmacy degrees and 15 Doctor of Pharmacy degrees.

Session of 1895–1896.

The length of the course was extended to two sessions of $7^1/_2$ months each.

The thesis requirement for graduation from the two-year course was discontinued.

A "postgraduate" course leading to the degree of Doctor of Pharmacy (Phar.D.) was offered for the first time. It consisted principally of advanced laboratory work in the subjects of the two-year curriculum and covered a period of 32 weeks of 5 full days each.

Session of 1896–1897.

The two-year course was extended in length to two sessions of 32 weeks each. The apprenticeship requirement for graduation was discontinued.

Session of 1900–1901.

A separate and distinct course, including laboratory work in dispensing pharmacy was added; also a course in commercial pharmacy.

Beginning with this session, the degree of Doctor of Pharmacy (Phar.D.) was conferred upon the completion of the two-year course, and the conferring of the degree of Graduate in Pharmacy (Ph.G.) was discontinued until the session of 1914–1915, when the recommendations of the American Conference of Pharmaceutical Faculties relative to standardization of degrees was adopted.

Session of 1906–1907.

The entrance requirements were advanced to the completion of 1 year of high-school work or its equivalent.

Session of 1913–1914.

Courses in Pharmaceutical Arithmetic, Pharmaceutical Latin and Pharmaceutical Jurisprudence were added to the curriculum.

Session of 1914–1915.

Beginning with this session, the requirements for eligibility to receive the degree of Doctor of Pharmacy (Phar.D.) were advanced to the completion of 3 years of specified work, and the degree of Graduate in Pharmacy (Ph.G.) was conferred upon the completion of the two-year course.

Session of 1918–1919.

A minimum of 2 years of high-school work was required for entrance.

Session of 1919–1920.

The conferring of the degree of Doctor of Pharmacy (Phar.D.) upon the completion of three years of work was discontinued and the degree of Pharmaceutical Chemist (Ph.C.) was given in its place.

Session of 1920–1921.

The entrance requirements were advanced to the completion of 4 years of standard high-school work or its equivalent, *viz.:*

"The applicant must be not less than seventeen years old and must have completed a four-year standard high-school course, or its equivalent. The course, or its equivalent, must have included one year of Latin. Two years of Latin, however, are more desirable.

Admission to the course in pharmacy is by certificate issued by the State Department of Education, 210 W. Madison St., Baltimore, Md. The certificate is issued on the basis of credentials, or by examination or both. Evaluation of credentials can be made by the Department of Education only, and all applicants, whether their entrance qualifications are clearly satisfactory as per the requirements for matriculation outlined above, or not, must secure a certificate from said Department of Education to be presented to the Dean before they can be matriculated."

Session of 1921–1922.

The curriculum was broadened to include the general educational subjects, English, Modern Languages, Algebra, Trigonometry and Physics.

Session of 1923–1924.

The regular course of study was lengthened to three years of 32 weeks each. Upon the successful completion of the course, the diploma of Graduate in Pharmacy (Ph.G.) was given. The award of the Ph.C. degree was discontinued.

Provision was made for giving a fourth year of work leading to the degree of Bachelor of Science in Pharmacy (B.S. in Phar.). The work of the fourth year consisted of courses in Advanced Pharmacy, Dispensary Practice, Pharmacognosy, Physiological Chemistry, Serology and Immunology, Civil Government, Food and Drug Analysis, Clinical Laboratory Practice and Economics.

Session of 1931–1932.

A complete list of the subjects comprising the course of study for this session is given because it shows the advances made up to the present and the condition of the curriculum at the end of the period of transition from a course of three years to one of four years. The attempt to build upon the old three-year course with a view to preparing the way for the final step in the change is readily discernable. The excessive amount of work now required in the first three years and the illogical sequence in which some of the subjects are scheduled are conditions brought on by this building process. The manner in which these conditions have been improved is shown in the outline for the new four-year curriculum.

OUTLINE OF PRESENT CURRICULUM.

First Year.

	First Semester.	Second Semester.
Botany *1s*, Structural	..	3
*Chemistry *1y*, Inorganic and Qualitative Analysis	4	4
*English *1y*, Composition and Rhetoric	3	3
*Modern Language *1y*, German or French	4	4
*Mathematics *1f*, Algebra	3	..
*Mathematics *2s*, Trigonometry	..	3
Pharmacy *1f*, History of Pharmacy	1	..
Pharmacy *2s*, Pharmaceutical Mathematics	..	2
*Zoölogy *1f*, General	4	..
	19	19

Second Year.

*Chemistry 2*y*, Organic	4	4
Pharmacognosy *1f*, General	4	..
Pharmacy *3y*, Galenical	4	4
*Physics *1y*, General	4	4
Physiology *1f*, Physiology and Hygiene	3	..
Chemistry *3s*, Quantitative Analysis	..	3
Pharmacology *1s*, Pharmacology, Toxicology and Therapeutics	..	3
	19	18

Third Year.

Bacteriology *1f*, General	4	..
Bacteriology *2s*, Serology and Immunology	..	2
Chemistry *4f*, Medicinal Products	4	..
Chemistry *5s*, Pharmaceutical Assaying	..	4
Pharm. Economics *1f*, Bookkeeping and Business Methods	3	..
Pharmacology *2f*, Pharmacology, Toxicology and Ther.	3	..
Pharmacy *4y*, Dispensing	4	4
Pharmacy *5y*, Pharmaceutical Practice	1	1
Pharmacognosy *2s*, Vegetable Histology	..	2
Pharm. Law *1s*, Pharm. Laws and Regulations	..	2
*Zoölogy *2s*, (elective), Vertebrate	..	4
	19	19

Fourth Year.

Chemistry *101f*, Medicinal Products	3	..
Chemistry *102f*, Food and Drug Analysis	4	..
Chemistry *103y*, Physical	3	3
Chemistry *104y*, Physiological	4	4
Pharmacy *101y*, Advanced	3	3
Pharmacology *101s*, Physiological Assaying and Testing	..	4
Elective	..	4
	17	18

Note: The letter following the numbers of a course indicates the semester in which it is offered: thus, course *1f* is offered in the first semester; *1s*, in the second semester. The letter "*y*" indicates a full-year course.

* Instruction in these courses is given by the faculty of the College of Arts and Sciences.

OUTLINE OF NEW FOUR-YEAR CURRICULUM.

Beginnir g with the session of 1932–1933, a minimum of four years of prescribed work will be required, the awarding of the diploma of Graduate in Pharmacy (Ph.G.) will be discontinued and the degree of Bachelor of Science in Pharmacy (B.S. in Pharm.) will be conferred upon candidates successfully completing the course.

First Year.

	First Semester.	Second Semester.
Botany *1s*, Structural	..	3
*Chemistry *1y*, Inorganic and Qualitative Analysis	4	4
*English *1y*, Composition and Rhetoric	3	3
*Modern Language *1y*, French or German	4	4
*Mathematics *1f*, Algebra	3	..
*Mathematics *2s*, Trigonometry	..	3
*Zoölogy *1f*, Invertebrate	4	..
	18	17

Second Year.

Botany *2f*, Pharmacognosy	4	..
Botany *2s*, Vegetable Histology	..	2
Chemistry *2y*, Organic	4	4
*English *2y*, Public Speaking	1	1
Pharmacy *1y*, Galenical	4	4
*Physics *1y*, General	4	4
Physiology *1s*, General	..	3
	17	18

Third Year.

Bacteriology *1f*, General	4	..
Bacteriology *2s*, Serology and Immunology	..	2
Chemistry *3f*, Medicinal Products	4	..
Chemistry *4s*, Quantitative Analysis	..	4
Economics *1s*, Principles of	..	3
Pharmacology *1y*, Pharmacol. Toxicol. and Therapeutics	3	3

Third Year.—Continued.

	First Semester.	Second Semester.
Pharmacy *2y*, Dispensing	4	4
Pharmacy *3y*, History of Pharmacy	1	1
Pharmacy *4f*, Pharmaceutical Mathematics	2	..
	18	17

Fourth Year.

(Required Subjects.)

Bacteriology *3s*, Hygiene and Sanitation	..	2
Chemistry *5f*, Pharmaceutical Assaying and Testing	4	..
Economics *2f*, Pharmaceutical	3	..
Law *1s*, Pharmacy Laws and Regulations	..	3
Pharmacy *5y*, Manufacturing Pharmacy	3	3
Pharmacy *6y*, Pharmaceutical Practice	1	1
Electives	7	8
	18	17

(Electives.)

Botany *3y*, Advanced Vegetable Histology	4	4
Chemistry *6y*, Physical	3	3
Chemistry *7y*, Physiological	4	4
Chemistry *8s*, Food and Drug Analysis	..	4
Pharmacology *2f*, Bioassaying	4	..
*Zoölogy *2s*, Vertebrate	..	4
Thesis		11

* Instruction in these courses is given by the faculty of the College of Arts and Sciences.

The attainment of the principal objective of the university schools is now only a short time off. With the inauguration of the minimum four-year course next fall, at all of the fifty-eight schools holding membership in the American Association of Colleges of Pharmacy, it is believed that the goal will have been reached.[1] And, in fairness to all, it should be stated that the independent schools have done

[1] A number of the schools have offered a four-year course leading to the Bachelor's degree for many years past. Some of these have also offered work leading to the advanced degrees, Master of Science and Doctor of Philosophy. At the present time 12 of the schools are requiring a minimum of four years of work for graduation.

their share of the work involved in bringing this about, and that no small amount of credit for the progress that has been made should be given to those pharmaceutical organizations not primarily concerned with educational matters but which have loyally supported this movement, namely: The AMERICAN PHARMACEUTICAL ASSOCIATION and the National Association of Boards of Pharmacy.

The necessity for some organized effort to properly develop pharmaceutical education in this country was early recognized by the AMERICAN PHARMACEUTICAL ASSOCIATION[1] but it was not until 1870 that the then existing schools took a united interest in the matter. In that year there was held in Baltimore a conference of delegates of the more progressive colleges of pharmacy for the purpose of bringing about uniformity in the standards for graduation.[2] The principal outcome of this conference was the formation of an organization of the colleges which continued to function until 1886, but which left no record of its activities or of its accomplishments, except some scattered notes in the minutes of the boards and faculties of the member colleges. A second organization of the schools was effected in 1900.[3] The organization formed at that time is now known as the American Association of Colleges of Pharmacy.[4] It has been a virile organization since the date of its birth and the leader in advancing the interests of pharmaceutical education. In the furtherance of its aims, it has been ably assisted by the National Association of Boards of Pharmacy which was organized in 1904 and with which it has many interests in common. In fact, the two organizations have worked hand in hand in advancing our standards to the position which they now occupy. Both labored earnestly and consistently in the endeavor to broaden the curriculum, to lengthen the course of study and to bring it up to the desired standards in other respects, but without definite progress before the War in Europe.

It seems that no less than an ultimatum from an outside agency was required to make us realize what was really the matter with our system of education and to spur us on to remedy its defects. The ultimatum was received on September 30, 1918, from an agent of the War Department. Dr. R. C. McLaurin, chairman of the whole Government educational plan, in a conference of pharmaceutical educators and others held in Washington, D. C., on that date relative to the establishment of Students' Army Training Corps in schools of pharmacy, declared: "If the colleges of pharmacy desire the same consideration accorded the other professional schools, they must demand of their students the same conditions for entrance and the same type of professional work required by these other professional schools."[5] Certainly, no declaration could have been more in keeping with the aims of the

[1] The AMERICAN PHARMACEUTICAL ASSOCIATION has taken an interest in pharmaceutical education from the very beginning of its existence in 1852. In 1887, it organized a section on pharmaceutical education, which is still continued as the Section on Education and Legislation.

[2] The call for this conference was issued by the Maryland College of Pharmacy. "Proc. Am. Conf. Pharm. Faculties," 1906, page 8.

[3] An unsuccessful attempt to form a new conference was made by James H. Beal and George B. Kauffman in 1893. The call for the conference of 1900 was issued by Henry P. Hynson, secretary of the Maryland College of Pharmacy. *Ibid.*, page 9.

[4] Previous to 1925, the title of the organization was The American Conference of Pharmaceutical Faculties.

[5] Rudd and Fackenthall, "Pharmaceutical Education," Bur. of Education, Dept. of the Interior, 1921, Bull. No. 11, page 12

university schools, and in my opinion it was the factor largely responsible for the progress made since the War and for the present trend in formulating our courses of study.

One of the immediate effects of the foregoing declaration was to create a more widespread interest in pharmaceutical education and to set the pharmaceutical educators, in particular, to searching for the best way of meeting the requirements laid down therein. It was soon realized that the problem was one that could not be hastily solved. There was so little upon which to build. Of course, the nature of the work done by the schools was known and likewise the nature of the requirements of the state boards of pharmacy for licensure, but there were practically no available data that could be used as a basis for defining the duties of a pharmacist and what he should know to be able to perform those duties satisfactorily. The collection and classification of data of this character was recognized as being the first step in the logical development of a new pharmaceutical curriculum. Fortunately for pharmacy, an outside agency came to its assistance, namely, the Commonwealth Fund. A subvention was granted by this fund through its Committee on Administrative Units to defray the expenses of a study of pharmacy. The study was conducted over a period of approximately three years under the direction of Doctor W. W. Charters, then of the University of Pittsburgh, and the results were made available in a comprehensive report published in 1927.[1] The data supplied by this report, together with the information collected by the Syllabus Committee,[2] a joint committee of several of the national pharmaceutical organizations which has functioned since 1906 in the preparation of the Pharmaceutical Syllabus, have been extensively drawn upon in planning the new curriculum for the School of Pharmacy of the University of Maryland as outlined on page 500 and have no doubt been utilized to a like extent by the other schools.

A new syllabus is now in the process of preparation and, if the tentative draft distributed last summer may be taken as an indication of the changes to be looked for, the pharmacy curriculum of the immediate future will show unmistakable signs of a drift to university standards. This will manifest itself mainly by the inclusion of a number of new courses. In addition to the established courses in pharmacy, there will probably be offered courses in English, public speaking, modern languages, mathematics, history, economics, psychology, zoölogy, pharmacology, hygiene and sanitation, public health, etc., and the schedule of studies will be arranged to give the student some time for specialization in at least one branch of the pharmaceutical or allied sciences.

Taken all in all, it is believed that the new curricula, in spite of the variations which will appear in them due to a difference in viewpoint or conditions of the

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[1] "Basic Material for a Pharmaceutical Curriculum." The McGraw-Hill Book Company, Inc., 1927.

[2] The Syllabus Committee is an outgrowth of a committee appointed by the Board of Regents of New York in 1905 to determine what should be the proper standards for the registration of schools of pharmacy in that state. In 1906, an invitation was extended to the National Association of Boards of Pharmacy and The American Conference of Pharmaceutical Faculties to be represented on the committee by one member from each organization. Since 1910, the committee has been composed entirely of delegates from pharmaceutical organizations, namely: The AMERICAN PHARMACEUTICAL ASSOCIATION, Association of Colleges of Pharmacy, National Association of Boards of Pharmacy. "Pharm. Syllabus," 3rd Edit., 1922, page 6.

individual schools, will be found to have been built upon good foundations and to have been developed logically. Students who complete the courses of study comprising them will have had a liberal as well as a professional education and there should be no question as to their ability to make for themselves a dignified place in our social system and to advance the prestige of pharmacy.

THE PRESCRIPTION DEPARTMENT.*

BY FRANK A. DELGADO, U. S. DEPARTMENT OF COMMERCE.

The prescription phase of the National Drug Store Survey has not been approached merely from the commercial angle. At no time was sight lost of the fact that the professional side of pharmacy is just as individual as the practice of medicine, dentistry or any other profession. It is true that the first and other reports of the Prescription Department will point out the benefits to be derived through greater standardization and uniformity and the adoption of modern merchandising methods, but the necessity of pharmacy operating under certain minimum requirements and rendering special and vital service to the physician and the public was and is fully realized.

The commercially minded pharmacist should not minimize the contribution which the science of pharmacy makes to his success. At the same time merchandising, when defined broadly as the application of business principles to any activity involving buying and selling, cannot be overlooked by the most professional. Such principles apply in filling prescriptions as in other phases of the business.

This becomes apparent as soon as a summary is made of the factors and business practices to which the successful operation of professional pharmacies can be attributed. Among these factors of success are:

(1) Knowledge, skill, experience, honesty, diligence and personality of both proprietor and staff.
(2) Physicians' support, coöperation, confidence and friendship.
(3) Location, accessibility to physicians.
(4) Store arrangement, adequate equipment, appearance and cleanliness.
(5) Buying carefully, quality, variety, purity and freshness of stock.
(6) Selling, accuracy in filling prescriptions, reasonable prices commensurate with quality and service.
(7) Service, every possible facility, such as private telephones, switchboards, rapid calling for and delivering of prescriptions, filling prescriptions without delay, prompt attention to mail orders, having on hand new foreign and domestic preparations.
(8) Advertising or promotion, continually contacting the physician, meeting with and speaking before physicians and internes, furnishing prescription blanks.
(9) Bookkeeping, adequate records, annual inventory and profit and loss statement, careful extension of credit, collect bills promptly.

Nearly all of the factors enumerated above embrace the two outstanding phases of merchandising, cost control and sales promotion. It is the latter phase only that is dealt with in the report just released by the Bureau of Foreign and Domestic Commerce and entitled "Prescription Sales Analysis in Selected Drug Stores." In addition to the sale report there will be two additional reports, one a companion to the report already referred to, but dealing with cost control, and another dealing with both cost control and sales promotion in professional pharmacies.

The material contained in the report already published is presented to the 60,000 retail druggists throughout the country in the hope that it will prove a basis of increased efficiency in the operation of the prescription departments of many of their stores.

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* An address before the National Drug Store Survey Conference, April 26, 1932, by Frank A. Delgado, U. S. Department of Commerce.

This report endeavors to show the important basic position the prescription department occupies in the operation of the retail pharmacy and points out opportunities for the proper application of both professional skill and modern merchandising methods.

Careful treatment is accorded the professional phase through the detailed study of nearly 24,000 prescriptions, their ingredients and the requirements of their compounding. The list of leading ingredients (161) reveals the extent to which the ingredients prescribed are chemicals or galenicals. Incidentally the bulk of them were official (listed in U. S. P. or N. F.) and should be of value to the pharmacist in building his prescription stock.

At the 1930 AMERICAN PHARMACEUTICAL ASSOCIATION Convention, pharmacists were called upon to institute adequate records for showing the total number of prescriptions filled, including refills, so that the extent of this phase of professional practice might be available for study.

A drug store could be mentioned that has filled over a million prescriptions, whose pharmacists are able to glance at their records and obtain at a glance the number of prescriptions filled for any given period, their total value for both new and refills, the average price and the daily value. Comparisons with the previous years' monthly totals are made and, if there is any evidence of business falling off, the matter is looked into so that the condition may be corrected, if possible.

The proprietor of a drug store may not need to keep a set of books devoted to the prescription department, but it is highly desirable that he know what his prescription stock inventories, and from them a detailed analysis of every phase of operation should be made. There are too many prescription departments that are not given a fair chance.

Let us see if we cannot point out how some of the facts and figures contained in this report will prove of practical value to the pharmacist, the wholesale druggist, the manufacturer, the schools of pharmacy and the approximately 2500 students that are said to graduate from these schools every year. There follow some of the answers to the questions most frequently asked regarding the prescription phase of the National Drug Store Survey.

(*1*) *What percentage of the drug store's volume is accounted for by the prescription departments?* It has been found in this survey to represent nearly one-fifth of the total sales volume of the independent drug stores studied when both prescription and non-prescription sales made out of the prescription department are combined. The range, however, is very wide.

(*2*) *Which drug stores, those with large or small sales volume, have a higher percentage of their income in prescriptions?* Drug stores with a smaller sales volume usually do a larger prescription volume in proportion to their total sales, the reason being that the prescription department as a rule does not lend itself to expansion to as great an extent as the commercial departments. This is illustrated by the fact that prescriptions only represented 3.12 and 1.58 per cent, respectively, of the total sales volume of the two chain stores studied—the stores with by far the greatest total volume; the leading five independent stores doing a volume of from approximately $47,000 to $77,000 a year had a prescription volume ranging from approximately eight per cent to fifteen per cent of the total sales. These percentages are for prescriptions alone and do not include other prescription department sales.

(3) *How can the pharmacist increase prescription department volume, or utilize the prescription department as a means for increased volume in other professional departments?* The possibilities for increased sales and profits in the prescription department and professional departments are so many that they could be made the subject of a lengthy article. Without counter-prescribing, the pharmacist could well use his professional knowledge to suggest to those customers having prescriptions filled, the purchase of such auxiliary items as fever thermometers, hospital and first-aid supplies, hot water bottles, ice caps, rubbing alcohol, disinfectants, deodorants, fumigators, baby, diabetic and invalid foods and numerous other items. The nature of the prescription would suggest the item indicated.

(*4*) *What other possibilities for prescription department sales expansion exist, that will keep the pharmacist busy and allow him to exercise his professional knowledge?* The pharmacist has an average of 1500 or from 900 to 2200 different drugs, chemicals and galenicals in the laboratory. An analysis of ingredients used in filling prescriptions that will be referred to later on reveals that only from approximately 500 to 800 of these are actually employed in filling prescriptions. Of course, the disparity between the two sets of figures is partially accounted for by the fact that the inventory records as a separate item, any chemical, drug or preparation in each of its forms, sizes, etc., whereas the ingredient compilation conversely lists a substance as a single item, regardless of

the number of different sizes or whether it was in powdered or crystal form. The pharmacist is placed in a very favorable position to sell disinfectants, insecticides, raticides, furniture and metal polishes, dry cleaners, bleaching solutions and numerous other preparations. Apparently, pharmacists have in many instances side-tracked these items for other merchandise that are far removed from pharmacy.

(*5*) *What other sales are made from the prescription department other than actual prescriptions?* Bulk sales of crude drugs, chemicals, galenicals, essential oils and manufacturers' specialties, such as gum arabic, cinnamon bark, oxalic acid, bismuth subnitrate, ammoniated mercury ointment, syrup of white pine and tar, elixir of digestive compound, argyrol solution, ichthyol, calomel tablets, quinine capsules. To determine approximately the extent of these non-prescription sales a check was made for 50 days in Store 1. During the 50 days the prescription department had 1830 non-prescription sales, an average of 36.6 such sales a day. The average value per sale was found to be 27.6 cents, these sales amounting to an average of $10.10 a day, or $504.77 for the 50-day period.

It is believed that the customer would frequently buy large amounts of these items if the pharmacist pointed out that a saving could be effected thereby.

(*6*) *How can the pharmacist attract attention to his prescription and professional departments?* One way is by substituting some educational or professional windows for the stereotyped commercial window displays that are seen so frequently these days. Display those old symbols of pharmacy, the gilded mortar and the show globe. Do not only prepare such a display once a year on National Pharmacy Week, but have them often. Take for example an outstanding Tennessee drug firm. This firm does a good fountain, luncheonette, cigar, candy and toilet preparation business, nevertheless, special emphasis is laid upon the prescription department in their window dressing and at least one street window at all times is devoted to their prescription department. On November 27, 1931, this store filled its millionth prescription. Prescription No. 1 was filled late in 1912.

In Trenton, N. J., an enterprising druggist builds good-will by sending with every prescription for a child a little puzzle to keep the child amused. This same druggist asks his customers whether the doctor specifically recommended his store and, if so, he mails the doctor a letter of thanks.

(*7*) *What was the average minimum and maximum number of prescriptions filled per day?* The 13 stores filled an average of 15.3 prescriptions per day, of which 3.9 were refills and 11.4 new prescriptions. The new prescriptions were divided 9.7 or 85 per cent non-narcotic and 1.7 or 15 per cent narcotic. However, there was a considerable range in these figures from store to store. For example, in the case of total new prescriptions, the range was from 24.9 daily in Store 1 to 4.4 in Store 11.

(*8*) *Did this include refills?* Yes, there was an average of approximately four refills per day. Refills accounted for 25 per cent of the total. However, refills varied from approximately 10 per cent to 45 per cent of the total number of prescriptions filled. Those stores that had been in business a long time usually led in refills. Also, the stores located in a higher income community led in number of refills.

(*9*) *What was the maximum number of prescriptions filled per day?* Four of the stores filled approximately 20, 22, 31 and 40 prescriptions per day. The store filling 40 prescriptions per day was a chain.

(*10*) *What was the minimum number of prescriptions filled?* Three of the stores filled from 6.2 to 6.5 prescriptions per day.

(*11*) *What was the average price charged for all prescriptions?* The average price charged for all prescriptions was $.92. However, this varied; for example, this average was $.91 for all non-narcotic prescriptions and $.97 for narcotic prescriptions. Then again the non-narcotic prescriptions were priced at only $.84 when all the ingredients were *official, that is, U. S. P. or N. F.* Non-narcotic prescriptions that contained a combination of both official and specialty ingredients were about ten per cent higher, or $.93, whereas, non-narcotic prescriptions that consisted only of *specialties were $1.02* or about 22% higher.

There was not a great variation in narcotic prescription prices regardless of whether the ingredients were official, specialty or a combination of these two classes.

(*12*) *What were the average prices charged for new and refill prescriptions?* New prescrip-

tions averaged $.95 each and refills averaged $1.00 each. The reason for this is the tendency of customers to order a larger quantity when obtaining refills. It was found that the druggist often pointed out to the customer that a saving could be effected by having the prescription doubled, if the customer intended to use the medicine over a long period.

(*13*) *Was the location of the store, type of customer served, or its sales volume responsible for difference in price charged?* There seemed to be no indication for the wide variation in prescription prices charged other than management. However, stores numbers 1, 2, 4 and 7 located at the intersections of main traffic arteries received prices above the average.

(*14*) *What relation, if any, is there between number of prescriptions filled and prices charged?* It was found that as the number of prescriptions filled increased, so did the average prices charged. There were only two exceptions among the 13 usual commercial type stores studied. The explanation for this would at first appear to be that the more prescriptions filled, the greater likelihood of the store taking on the aspect of a professional store, and as a consequence handling and dispensing a large proportion of high priced domestic and foreign specialties. In the two exceptions noted, one was a chain store and while, in number of prescriptions filled, it was the lowest store but three, it was the fifth highest in price. This store carried a wide variety of items in the prescription department, due to the fact that they filled very few prescriptions from the same doctor. The approximate 2000 prescriptions studied in this store were written by 551 doctors, whereas, 5500 prescriptions studied in a professional store nearby were written by only 444 doctors, and 3500 prescriptions studied in another professional store in the same neighborhood were written by only 250 doctors. The other exception was a store that filled the lowest number of prescriptions of all 13 stores, but charged the second highest average price. This store did not carry a wide variety of ingredients in its prescription department, nor did the neighborhood warrant above average prices. The price policy was obviously one of individual management.

(*15*) *Was there any difference in price policy between the usual commercial type stores and the professional stores?* The facts regarding the professional store will be published in a separate report. However, there was evidence that the prices set by professional stores were based to a greater degree on the cost of ingredients. The average price charged by the two professional stores for non-narcotic *U. S. P. and N. F. prescriptions* averaged only $.67 and $.80 each as against $.84 for the same type of prescriptions for the usual commercial type store. However, the professional stores charged an average price of $1.04 each for specialty prescriptions against an average price of $1.02 each charged by the other stores. Some specialty prescriptions present a pricing problem to drug stores, inasmuch as department stores carry them and feature them as loss leaders.

(*16*) *What was the usual price charged for prescriptions?* Over 57 per cent of the 24,000 prescriptions studied were priced at from $.75 to $1.00, thus clearly showing this price range to be the most usual. Approximately twenty per cent were priced from $.50 to $.70. Eighteen per cent were priced at from $1.05 to $1.50 and approximately four per cent were priced at over $2.00. Or it might be stated that only 21 per cent of the 24,000 prescriptions studied were priced at over $1.00. The narcotic prescriptions generally were priced somewhat higher than the non-narcotics. Only 12.51 per cent of the narcotic prescriptions were priced below $.75, while 22.86 per cent of the non-narcotic prescriptions were so priced.

(*17*) *Were there any examples of abnormally low priced prescriptions?* Out of approximately 24,000 prescriptions analyzed, 610 or 2.54 per cent were priced at less than 50 cents. Of the 610 prescriptions referred to above, 565 were non-narcotic and 45 were narcotic. Of this minimum price group, 19 were priced at $0.10, which includes one narcotic; 55 were priced at $0.25 which includes 6 narcotics; 39 were priced at $0.30; including three narcotics; 159 were priced at $0.35 including 18 narcotics and 338 were priced at $0.40 or $0.45 including 17 narcotics.

While it is realized that it is difficult in a number of cases to charge more than a nominal sum for an extremely simple prescription, it is believed that the pharmacist frequently loses sight of the fact that even the simplest prescription involves an exercise of professional knowledge and that more consideration should be given to elements of cost in handling which are the same on every prescription transaction.

(*18*) *Were there many prescriptions selling for over $2.00?* Of the nearly 24,000 prescriptions studied, only 96 were classified as high priced prescriptions, that is, prescriptions selling for $2.00 or more

Most of the high priced prescriptions were sold at from $2.00 to $4.00. However, while these were the more common high priced prescriptions, there were a few prescriptions which were considerably more expensive, one selling for as high as $11.50. However, only 3 of the 96 prescriptions were high priced because a large quantity was sold.

Fifty-nine of the 96 high priced prescriptions were proprietaries. High priced prescriptions were sold in stores of largest sales volume having customers with greatest purchasing power. Four stores, together, accounted for more than half of the high priced prescriptions sold.

(*19*) *Were there any examples of marked prescription price inconsistencies?* Yes, there was found to be a wide variation in price based more on size than on cost of ingredients. For example, in one store the charge for a prescription consisting of Codeine Phosphate grains 16, Syrup of Thiacol ounces 1, and Syrup of Premocal Q. S. ounces 3, was only $1.25. This was obviously too low. The same store filled a prescription for Tincture of Opium drachms 2 and Milk of Magnesia ounces 8 at a charge of $1.40. The quantity was nearly three times greater than the first prescription but the cost of ingredients much less. There was another instance where one store charged $.60 for a prescription of 20 tablets of a specialty nature, while another store charged $.75 for 40 of the same tablets.

The discussion of another angle of price information that we have compiled will be discussed in a future report, and that is price according to form, size and contents. We have an elaborate table showing the average price of liquid prescriptions according to contents and whether official, specialty or mixed. We have the same information for capsules, ointments, suppositories, charts, and bulk powder, prescriptions, etc. For example, an examination of this table would show that all stores charged from six to fourteen cents more for a four-ounce liquid specialty prescription than for a four-ounce liquid official prescription, and from two to thirty-four cents more for a twelve-capsule specialty prescription than for a twelve-capsule official prescription.

This report will also record certain price discrepancies and recommendations will be made regarding a cost and price method that it is hoped will reduce their number.

(*20*) *In what form are prescriptions in greatest demand?* It was ascertained that 61.29 per cent of the prescriptions were liquids. An even slightly greater per cent of the non-narcotic prescriptions were liquid in form, but a smaller per cent of the narcotic prescriptions were liquids, although this was the most used form for narcotics.

The form which was the second most popular was capsules, which comprised 17.51 per cent of all prescriptions. However, capsules were used in 40.12 per cent of the narcotic prescriptions, being the form used in nearly as many cases as was liquid.

Tablets were used in 9.91 per cent of the prescriptions, the percentage being a little higher for the non-narcotics but amounting to only 7.84 per cent of the narcotic. Thus it will be seen that these three forms of prescriptions, liquids, capsules and tablets, accounted for approximately 89 per cent of all prescriptions, and 95.95 per cent of the narcotic prescriptions.

Ointments account for 3.8 per cent, divided powders for 3.3 per cent, bulk powders for 1.5 per cent, effervescent salts for 1.3, pills for approximately 1 per cent, suppositories for less than one-third of 1 per cent. The remaining one-fifth of 1 per cent was divided among a miscellaneous group consisting of konseals, platers, globules, pearls, crude drugs, etc.

It has not been customary to think of the prescription filling operations of a drug store as constituting an impressive manufacturing industry. Liquid prescription in the U. S. averaged four ounces each and 61 per cent of all prescriptions filled were liquid. It would appear from these figures and the estimates as to number of prescriptions filled that production in the retail drug stores would amount to approximately 1,000,000 gallons.

It has been suggested that schools of pharmacy may find the information regarding form of practical value in their course in operative pharmacy.

(*21*) *What quantity of liquid was most frequently presented?* The 4-oz. size was easily the most in demand, representing 27.48 per cent of the liquid prescriptions. The 3-oz. size was a close second in sales. These two sizes together accounted for nearly half of the liquid prescriptions. The 1-oz., 2-oz. and 6-oz. sizes were the only other sizes of outstanding importance, together accounting for 37.04 per cent of the liquid prescriptions. All of the other sizes together represented only 13.62 per cent of the liquid prescriptions studied.

An example of the practical application that can be made from this information follows: A manufacturer of bottles and other glassware recently offered a deal whereby with every order of

ten or more cases of prescription ware, a set of three double-scale graduates would be given free. On the above analysis of liquid prescriptions according to size, it is possible to state that 10 of the 13 stores could have used one or more of these deals in one year or less for prescription alone. In a future report the liquid prescriptions should be broken down further into eye solutions, emulsions, lotions, liniments and other liquids.

(*22*) *Is it true that the compounding of prescriptions has become a mere pouring out of a liquid or counting out a certain number of pills or tablets?* Just the contrary is indicated, the survey shows that 65 per cent of the prescriptions call for more than one ingredient. Over 4 per cent of the prescriptions called for six or more ingredients.

Narcotic prescriptions were found to average 3.2 ingredients each whereas non-narcotic prescriptions averaged only 2.4 ingredients each.

(*23*) *To what extent is skill and knowledge required in compounding prescriptions?* It is true that prescribing habits have changed. Prescriptions calling for a large number of ingredients are not as common. There are fewer prescriptions for hand-made pills, complicated suppository formulas, emulsions, and odd fluid extracts. As a consequence pharmacists are relieved of some of the responsibilities that were formerly theirs in the matter of incompatibles and doses. On the other hand they have taken on new and important duties in that they are called upon to supply much information of a scientific order that involves a knowledge of physiology and physiological chemistry. They must know gland products, biologicals, ampoules and scientific specialties.

It is difficult to determine exactly the skill required for various prescriptions. Even a prescription containing just one ingredient, and which might be considered to require no skill in compounding, really requires careful attention and judgment; the importance of the question of dosage alone cannot be underestimated.

(*24*) *Was the size of the empty capsule used always indicated?* Only a little more than one out of four capsule prescriptions indicated the size of capsule used. Indication of the size of capsule used or for that matter the powder paper and the size of the box in which powders are dispensed can well be considered a step toward greater efficiency, for it anticipates any possible customer criticism and loss of confidence in the pharmacist.

(*25*) *What percentage of the number of prescriptions studied were written in the metric system?* It was found that only 7.67 per cent of the prescriptions studied in 12 of the 13 stores were written in the metric system. Some of the stores studied were not equipped with a set of metric weights. Studies of the causes of inaccuracies in prescription compounding have at times pointed out as a major cause the fact that druggists not having metric weights and measures are liable to make mistakes when transcribing prescriptions written in the metric system to the apothecary system in compounding the prescriptions. Converting, like a pestilence, should be avoided when possible. Formulas written in the metric system call for the use of metric weights and measures. Actual use of metric weights will teach one to visualize the quantity of a drug or chemical that weighs a certain number of grammes, so that when one reads a prescription calling for this amount he will visualize it in metric quantities rather than the equivalent in avoirdupois or apothecaries weights or measures.

(*26*) *How many physicians wrote the prescription analyzed in each store, and what was the percentage accounted for by each?* A large proportion of the number of physicians writing the prescriptions studied wrote only one or two prescriptions each, for any one store. These doctors represented from 50 per cent to 70 per cent of the total number of physicians writing the prescriptions studied in any one store.

There were generally a few physicians individually writing a large number of the prescriptions studied. For example, in store 3-B, four physicians each wrote more than 100 of the prescriptions, and together the prescriptions of these four physicians represented 35 per cent of the prescriptions studied.

A special study was made in order to ascertain the extent to which each physician wrote prescriptions in 8 of the stores studied. The per cent of total prescription business accounted for by the 10 leading physicians in each store was fairly uniform for 6 of the 8 stores, ranging from 43.75 per cent in store 11-B to 58.35 per cent in Store 7-B, where a woman physician accounted for nearly 40 per cent of the prescriptions studied. However, the 10 leading physicians in Store 2 contributed only 21.02 per cent of its prescription business. This study shows quite clearly that most prescription departments depend quite largely on a small number of physicians for about

half of their business, the other half being written by more occasional physicians. Although three stores had from about one-fifth to one-quarter of their prescription business, as judged from the prescriptions studied, from the prescriptions of their leading physicians, none of them depended on a single physician for a great part of their business, with the exception of two of the stores, 13-D and 7-B.

This information would seem to indicate that it should not be difficult for the pharmacist to detail those physicians who write the majority of the prescriptions he fills in terms of products of his own manufacture, such as U. S. P. or N. F. preparations, or manufactures specialties.

These facts should also impress the pharmacist of the necessity of retaining the good-will of his leading physicians by rendering maximum service to their patients. It should also point out the desirability of cultivating the patronage of additional physicians, for, while every store naturally welcomes a large prescription business from any physician, nevertheless, a condition such as one or two physicians accounting for a good majority of the prescription business is a bit dangerous. The disastrous effects on the prescription department of a store in the event this physician suddenly ceased to practice can well be imagined.

(*27*) *Was the type of practice engaged in by physicians shown?* Yes, this was done for eight of the stores and, while no conclusion can necessarily be drawn, it is interesting to note that, in the eight stores studied, general practitioners wrote the largest number of prescriptions. In three of the stores, all of the 10 leading physicians were general practitioners, while most of them were general practitioners in several stores. In store 11-B there was nearly equal division between general practitioners, surgeons and physicians who were both surgeons and general practitioners; but the two leading physicians in the store's prescription business were general practitioners.

(*28*) *How many of the prescriptions studied were difficult to read?* Approximately 750 or 3.13 per cent of the prescriptions studied registered poor legibility and 76 per cent were recorded as fair. Poor legibility is a costly factor as it often delays the filling of a prescription until the druggist can communicate with the doctor. Where two words are quite similar, poor legibility might at times lead to the use of the wrong ingredient.

An interesting case that might be mentioned was where a physician wrote a single ingredient prescription. The directions read "as directed," the item appeared to be Lysol. Everything was apparently in order. But this pharmacist made it a point to always ascertain if his customers clearly understood the use of the drug, or drugs, when only "as directed" was written. Upon questioning it developed that Laxol was intended and the patient was to have taken a tablespoonful. The pharmacist's care in this instance may have saved a life. The incident not only points out the importance of the physician writing legibly, but likewise the fact that the use of the term "as directed" should be employed sparingly. This is a subject that might be advantageously discussed in joint meetings attended by pharmacists and physicians.

(*29*) *Do physicians specify any particular brand when prescribing galenicals?* Only slightly more than one per cent of all prescriptions studied specify the galenicals of any particular brand, or firm. It should be clearly understood that this tabulation does not include manufacturer's trade name, pharmaceutical specialties, but only such galenicals as, for example, tablets of acetphenitidi, elixir of digestive compound, etc.

(*30*) *To what extent do physicians dispense their own medicines in the country?* A report entitled "Wholesaler-Retailer Relation Study for Druggists" to be released shortly after the drug store survey field work is completed will state that. In towns with a population of less than 3000, nearly one-third of the drug dispensing is by physicians, while in towns of more than 12,000 inhabitants very little or no dispensing by physicians was found in a majority of cases, although such dispensing was considerable even in some of these larger towns. In a report entitled "The Costs of Medicines" recently released by the Committee on the Cost of Medical Care it is stated that $25,000,000 worth of medicines are dispensed annually by physicians.

(*31*) *To what extent do physicians dispense their own medicines in large cities?* It was not possible to determine the exact number of physicians in the city of St. Louis who do their own dispensing. However, certain drug manufacturing houses gave the following information and, while not inclusive of all dispensing physicians, it will show that there is still considerable dispensing by physicians in that city. One manufacturer sells only to 50 doctors whose volume of business is enough to justify a salesman's call. Another firm sells to about 200 dispensing doctors in the city.

Another firm, the activities of which are almost entirely among dispensing physicians, the firm doing very little business with retail drug stores, had a list of 349 dispensing doctors in St. Louis, but even this list was not claimed by the firm to include all of the dispensing physicians in that city. To show what proportion of the total number of doctors in St. Louis do their own dispensing, it might be stated that there are more than 2000 doctors in the city. The most complete list contained 2346 names, and included institutional men and professors at the medical schools.

(*32*) *How many ingredients were used in filling the prescriptions studied in each store?* There was an average of 608 ingredients, of which 39.7 appeared but once and an additional 15.2 only twice.

(*33*) *Did the number of ingredients used vary directly with the number of prescriptions filled?* Not necessarily; for example, one of the stores, a chain, that stood tenth in number of prescriptions filled, ranked second in number of ingredients used, having employed 682 different ingredients in the filling of 2000 prescriptions. This is accounted for by the fact that the prescriptions studied in this store were written by 549 physicians, or an average of less than four prescriptions per physician.

Another store that stood high not only in number of prescriptions filled, but in percentage of total sales volume, used the smallest number of ingredients of any store excepting one. This store draws a large share of its business from physicians whose offices are nearby.

It is thus clearly shown the necessity of carrying a wide variety of ingredients is in ratio to the variety of the physicians writing the prescriptions, rather than the volume of prescription business.

(*34*) *What was the relation between the number of ingredients used in filling prescriptions and the number of items stocked in the prescription department?* There was approximately one different ingredient used in filling the prescriptions studied for every three stocked in the prescription department.

All of the stores had the same inventory problem. The number of ingredients used in filling the prescriptions studied accounted for only an average of 37 per cent of those stocked in the prescription department. However, this varied from 28 per cent in one store to 54 per cent in another store. It is interesting to note that the store with only 28 per cent had the highest prescription volume of any store studied. There is no logical explanation for his prescription stock so far exceeding his prescription requirements, other than it is an old store and probably has an accumulation of slow-moving prescription items. The same explanation might be offered for the 54 per cent store. This was a new store in a modern residential district; it stood fifth in prescription sales volume.

A portion of this disparity between the number of ingredients dispensed in prescriptions and carried in stock is accounted for by the fact that there are sometimes two or more brands of the same item stocked. Also in the case of tablets as, for example, calomel or strychnine tablets, there are several different strengths, such as from $^1/_{10}$ of a grain to 2-grain calomel tablets. Chemicals are found in powdered or crystal form. Another reason is that the same item may be duplicated in two or three sizes, such as a handy container for convenience and a larger bottle or package containing a surplus supply. Then again it must be recalled that a large number of items stocked and sold out of the prescription department are not necessarily dispensed in prescriptions, for example, essential oils and crude drugs.

(*35*) *How many items were stocked in the prescription department and what proportion of the total did they account for?* There was an average of approximately 1500 items stocked in the prescription department as against 5070 for the store as a whole, or 29 per cent of the total items stocked were in the prescription department. The number of prescription items varied from approximately 900 to 2200. The number of items stocked was more or less in ratio to the prescription volume. However, there were a number of exceptions, the most outstanding being a store filling 6 prescriptions a day, and having only a 6 per cent prescription sales volume. This store carried 1562 different prescription items.

In comparing the number of items in the prescription stock with other drug store departments or the store as a whole, it should be borne in mind that items, not units, are being compared; for example, one gross of liver pills or tooth paste is only one item.

Any discussion of the number and variety of items in a prescription department should take

cognizance of the definite changes that have taken place in the study and practice of medicine and their effect on pharmacy.

These changes have no doubt affected the character and variety of ingredients and it would seem reasonable to expect to find a very much larger range of items in a store of some age than a newer store. The thought suggests itself that where the long established pharmacy finds its prescription inventory top-heavy that it would be warranted in disposing of at least from one to five per cent of the number of items stocked, thereby gaining, if nothing else, some valuable shelf space.

(*36*) *Will it be possible to show the total amount invested in the inventory of the prescription department of each store?* Figures available for four of the independent stores show that the prescription department inventory accounts for, on an average of, one-sixth of the total inventory or for these four stores an average prescription stock inventory of $1140 against $6800 total inventory. The prescription stock investment of these four stores ranges from $407.00 for a store with 913 prescription items to $1980.00 for a store with 2163 prescription items.

(*37*) *How was the prescription inventory investment divided among chemicals, galenicals, crude drug specialties, biologicals, essential oils, etc?* This question will be answered more accurately and fully in the second report. At present, based on figures for four stores, we find that specialties are responsible for from thirty to thirty-eight per cent of the prescription inventory investment, nor does this include specialties in tablet form which, when added, will probably bring the total up to from 35 to 45 per cent.

Galenicals not including tablets accounted for from 20 per cent to 30 per cent of the dollar inventory or an average of 24 per cent. Chemicals accounted for 11 to 14 per cent of inventory value.

The share of other items in the value of the prescription department inventory was as follows:

Biologicals accounted for from 2 per cent to 8 per cent, or an average of 4 per cent.

Glandular products accounted for from 4 per cent to 7 per cent or an average of 5 per cent. Incidentally some of these were of a specialty character.

Essential oils accounted for an average of approximately 2 per cent and botanical drugs for an average of $2^1/_2$ per cent, while ampules were not present in two of the stores, but accounted for 2 per cent each in the other 2 stores.

The remainder was accounted for by a few miscellaneous items not otherwise classified, and accounting for a little less than 1 per cent for each store.

The multiplicity of prescription items and the order of their occurrence, particularly specialties, shows clearly the necessity of the pharmacist keeping his figures in the right proportion to sales volume.

(*38*) *What are the leading ingredients used in prescriptions?* As has been previously stated for the purpose of the ingredient study, any ingredient which appeared 25 times or more in the 15,063 prescriptions studied in eight stores was considered a leading ingredient. A total of 1746 different ingredients were used in compounding these prescriptions and 230 or 13 per cent of them had an occurrence of 25 times or over. Of the 230 leading ingredients, 80 were chemicals, 81 were galenicals and 69 were proprietaries. Of the eighty chemicals, all were official (that is, U. S. P. or N. F.) except three. Of the eighty-one galenicals and miscellaneous drugs and preparations, all were official (U. S. P. or N. F.) except twelve. The majority of these were of a semi-official character, consisting in a number of cases of tablets or elixirs of official substances.

Twenty-four of the 69 specialties were found to have official equivalents, fourteen of which were included among the official chemicals and galenicals referred to above. The ingredients occurring 25 times or more are shown in the table contained in the printed report entitled Domestic Commerce Series—No. 61 "Prescription Department Sales Analysis in Selected Drug Stores" for sale by the Superintendent of Documents, Washington, D. C., price 5 cents. At this time it is gratifying to state that already this list has been put to practical use by a chemical manufacturer to check an assortment of 50 chemicals that they sell in a lot and recommended as being probably those most frequently called for.

CONCLUSION.

The pharmacist who takes pride in his profession and realizes that it is the prestige department of his business, the department that establishes confidence for him in the community, should, whether his prescription volume is large or small, whether it brings a profit or a loss, be

anxious to secure accurate data that will enable him to judge whether or not his prescription department is susceptible of improvement.

The value of the report will depend upon the use made of it. If the pharmacist looks it over casually, merely as of general interest, he is not apt to profit much by it. If it stirs in him a desire to find out how his store compares with the average in number of prescriptions filled, in prices charged, in ingredients used and required, in number of prescriptions from each physician, and instills in him the desire and necessity of compiling similar records based upon the transactions occurring daily in his own prescription department, then he is on his way to acquire knowledge that will not only make of him a better pharmacist but will prove remunerative.

Records to many druggists are just a meaningless set of figures. One definition of the word "record" is "the best performance." Incidentally, those druggists who keep record of their prescription transactions will generally be found numbered among those whose prescription business might be termed an outstanding performance.

ASSOCIATION MEETINGS.

"If a member of an association were to visualize results of applied ideas such as have been successfully used by other business men, he would not be apt to say, 'I will not have to go to the convention this year,' but rather, 'this is another year that I cannot afford to miss the chance of picking up something new.' The second reason is based on a lack of knowledge of what the convention can do and has done for business men in similar or comparable lines. If individual commercial and industrial organizations can afford to invest time and money of their employees in a three-day sales convention once a year, then the trade or professional associate should have no great difficulty in demonstrating the possible value of a trip to his annual convention."

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1931–1932.

Office of the Secretary, 10 West Chase Street, Baltimore, Md.

LETTER NO. 10.

April 14, 1932.

To the Members of the Council:

81. Tentative General Program for the Eightieth Annual Meeting. With the approval of President Adams, Local Secretary Stanbury and the Committee on Standard Program of the Council, the Secretary submits the following tentative general program. Officials of the various affiliated organizations represented in the program have approved those features in which their respective organizations are directly interested.

GENERAL PROGRAM FOR THE EIGHTIETH ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION AND RELATED ORGANIZATIONS, HOTEL ROYAL YORK, TORONTO, ONTARIO, AUGUST 15–27, 1932.

All dates included in special fare arrangements with railroads.

AUGUST 15–19TH.

Plant Science Seminar. *Program and Meeting Rooms to be arranged.

SATURDAY, AUGUST 20TH.

Morning and Afternoon.

National Conference on Pharmaceutical Research—Parlor A.

MONDAY, AUGUST 22th.

9:00 A.M. Council A. PH. A.—Club Room.
9:00 A.M. N. A. B. P.—P. D. R. 1–3.
9:00 A.M. A. A. C. P. Executive Committee—P. D. R. 4.
Chemistry Conference—Parlor A.
Pharmacy Conference—Parlor C.
Materia Medica Conference—Parlor D.
Pharmaceutical Economics Conference—P. D. R. 5
1:30 P.M. N. A. B. P.—P. D. R. 1–3.
1:30 P.M. A. A. C. P.—Library.
6:00 P.M. Dinner, N. A. B. P.
6:00 P.M. Dinner, A. A. C. P.
8:30 P.M. Reception—C. Ph. A., A. PH. A. and Related Organizations. (Addresses of welcome, etc., followed by dancing.)

TUESDAY, AUGUST 23RD.

9:00 A.M. Joint Meeting N. A. B. P. and A. A. C. P.—Banquet Hall.
1:30 P.M. First Session, House of Delegates—Banquet Hall.
2:30 P.M. N. A. B. P.—P. D. R. 1–3.
2:30 P.M. A. A. C. P.—Library.
6:30 P.M. Banquet, C. Ph. A., A. PH. A. and Related Organizations.

WEDNESDAY, AUGUST 24TH.

9:00 A.M. General Session, with Canadian Pharmaceutical Association—Banquet Hall.
2:00 P.M. First Session, Scientific Section—Parlor A.
2:00 P.M. First Session, Section on Education and Legislation—Parlor C.
2:00 P.M. First Session, Section on Historical Pharmacy—Parlor D.
2:00 P.M. First Session, Conference of Pharmaceutical Association Secretaries—P. D. R. 4–5.
4:00 P.M. Second Session, House of Delegates—Banquet Hall.
6:00 P.M. Dinner, Kappa Psi Fraternity.
6:00 P.M. Dinner, Rho Chi Fraternity, followed by annual convention.
6:00 P.M. Dinner, Lambda Kappa Sigma Sorority.
8:00 P.M. Moonlight Excursion.

THURSDAY, AUGUST 25TH.

9:00 A.M. Council A. PH. A.—Club Room.
9:00 A.M. First Session, Section on Commercial Interests—Parlor C.
9:00 A.M. First Session, Section on Practical Pharmacy and Dispensing—Library.
9:00 A.M. Second Session, Section on Historical Pharmacy—Parlor D.

9:00 A.M.	First Session, Conference of Law Enforcement Officials—P. D. R. 4–5.
12:00 M.	Veteran Druggists' Luncheon.
2:00 P.M.	General Session, with Canadian Pharmaceutical Association—Banquet Hall.
6:00 P.M.	Dinner, Phi Delta Chi Fraternity.
8:00 P.M.	Joint Session, Scientific Section and Section on Practical Pharmacy and Dispensing—Banquet Hall.
8:00 P.M.	Second Session, Section on Education and Legislation—Parlor C.
8:00 P.M.	Second Session, Conference of Pharmaceutical Association Secretaries—P. D. R. 4–5.

FRIDAY, AUGUST 26TH.

9:00 A.M.	Third Session, House of Delegates—Banquet Hall.
2:00 P.M.	Second Session, Scientific Section Parlor A.
2:00 P.M.	Second Session, Section on Practical Pharmacy and Dispensing—Library.
2:00 P.M.	Second Session, Section on Commercial Interests—Parlor C.
2:00 P.M.	Second Session, Conference of Law Enforcement Officials—P. D. R. 4–5.
6:00 P.M.	Special dinners.
7:00 P.M.	Final Session, House of Delegates—Banquet Hall.
8:00 P.M.	Final General Session A. PH. A.—Banquet Hall.
9:00 P.M.	Farewell Party—Convention Hall.
10:00 P.M.	Council A. PH. A.—Club Room.

SATURDAY, AUGUST 27TH.

All-Day Visit to Canadian National Exposition, which opens on August 26th.

(*Motion No. 30*) *It is moved by Kelly that the tentative General Program of the Eightieth Annual Meeting be approved.*

82. Use of Text of N. F. V. Motion No. 27 (see Council Letter No. 9, page 409) has been carried and Dr. Millar has been advised.

83. Membership in Inter-Society Color Council. Motion No. 28 (see Council Letter No. 9, page 409) has been carried and the Secretary of the Council has been advised.

84. Election of Members. Motion No. 29 (see Council Letter No. 9, page 410) has been carried and applicants numbered 214 to 275, inclusive, are declared elected.

85. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received.

No. 276, B. W. Kaplan, 8626 Cedar Ave., Cleveland, Ohio; No. 277, John W. Lee, George Washington University, Washington, D. C.; No. 278, George A. Moulton, Peterborough, N. H.; No. 279. M. W. Myers, 1410 W. 25th St., Cleveland, Ohio; No. 280, L. E. Ponder, Allen Bros., Henderson, Texas; No. 281, Raymond S. Smith, George Washington University, Washington, D. C.; No. 282, Bemis V. Spieth, 12801 Woodland Ave., Cleveland, Ohio.

(*Motion No. 31*) *Vote on applications for membership in the American Pharmaceutical Association.*

E. F. KELLY, *Secretary.*

LETTER NO. 11, APRIL 19, 1932.

To the Members of the Council:

86. Headquarters Building. The following letter has been received from Chairman Dunning and is dated April 13th:

"The question of the exact location of our building on the site will soon be determined by the Commission of Fine Arts and the National Capital Park and Planning Commission. It will be located either on a line with the Academy of Sciences building on the adjoining lot to the east, or slightly in advance of it, as may be found best suited to the plans for the Naval Hospital buildings to the west and between our site and the Potomac River. With the completion of the general plans for the Naval Hospital buildings and grounds, all of the available building sites facing on Constitution Avenue, between Seventeenth Street and the Potomac River, have been tentatively assigned—to the Pan American Annex, the Public Health Service, the Army, the Navy, the Academy of Sciences, the A. PH. A. and the Naval Hospital in order from east to west.

"It is now planned to widen Constitution Avenue to eighty feet and also to widen Twenty-third Street, which will place our building at the junction of these main traffic arteries to and from the Lincoln Memorial, the Arlington Memorial Bridge and the Mall.

"Senate Joint Resolution No. 50 to close Upper Water Street in our site; to authorize the transfer to the A. PH. A. of such an area adjoining the property it now owns, as may be required to locate its building, in accordance with the plans approved by the Commission of Fine Arts and the National Capital Park and Planning Commission; and requiring that the A. PH. A., in turn, transfer to the U. S. Government a strip seventeen feet wide along the west side of its property for the widening of Twenty-third Street, as an approach to the Lincoln Memorial, has passed the Senate and is now before the House of Representatives. As it has been approved by the Governmental Agencies interested, it is expected that it will pass the House as soon as the pressing tax and bonus legislation is disposed of.

"When this resolution has passed the House and been approved by the President, the last of the obstacles that have for so long delayed the construction of our building will be out of our way. And it may be pointed out that, while these delays have been very trying, they have added materially to the beauty and value of our location and have placed our building in surroundings that will protect it from change and deterioration. We have also profited in a direct way, as construction and upkeep costs have been materially reduced, at least twenty-five per cent, as shown by revised bids secured in January. In the meantime, there have been some further reductions and they may go still lower.

"Our architect, Mr. John Russell Pope, advises that we select a builder from the firms that are invited to bid, at this time, and enter into a contract with them, specifying the maximum cost of the building, giving the Association the value of any reductions in charges between those in effect at the time the revised bids were taken and at the time of construction, and protecting it against advances, should they occur. The contract also provides that it be in effect for one year and is not effective in that period if the Government, for any reason should hold up the project. Such a contract would seem to protect the Association fully. It is also Mr. Pope's opinion, as well as that of others we have consulted, that building costs are now about as low as they will probably go and that this is an ideal time to build, especially as the ASSOCIATION can be protected against decline and advance in cost.

"The lowest bid for the building was that of George A. Fuller Construction Company of New York, at $237,000, as of January 30, 1932. Mr. Pope's office has also secured bids on all additional work: fence around the site; sidewalks; landscape and planting; insurance; extra foundations to protect sewers, etc. These, with the remainder due on the architect's fee, will bring the cost to approximately $270,000.

"The specifications call for the use of limestone. In order to have all buildings in this area harmonize in exterior material, it may be necessary to use a more expensive grade of limestone or even some variety of marble. If so, the cost will be increased, but it is expected that further savings will fully offset such advance.

"The plans have been gone over a number of times and simplified as to design and cost. We have had the advice and helpful assistance of the Commission of Fine Arts, the National Capital Park and Planning Commission and others, for which we are greatly indebted, in bringing our plans into conformity with the ideals for the monumental buildings that are to occupy this choice area.

"The Headquarters Building Fund now totals $299,716.60, including the Treasury Bonds purchased on September 15, 1931. Two special funds, one of $5000, and the other of $2500 will furnish and provide up-keep of the furniture, etc., of the editorial offices and the secretary's office. Mr. Pope estimates that the additional furniture and fixtures required will cost from $10,000 to $15,000. The Procter Fund is ample for the Procter Memorial, and funds for other special objects are expected.

"It would seem then that we have in hand sufficient funds to erect and equip the building, including landscaping, planting and walks, with a balance for any contingencies that may arise. When the building is actually under way, we expect to collect, from unpaid subscriptions, an amount to endow the perpetual upkeep of the building on a basis advised by Mr. Pope as ample for the purpose.

"The building requires no elevator service, and automatic oil heating is provided. The maintenance charges will be reasonable, as tax exemption is expected for the building and site.

"Will you please place a motion before the Council that the President, Secretary and Treasurer be authorized to enter into a contract with the George A. Fuller Company for the erection of the building, in accordance with the general provisions of such contracts and with

the protection provisions mentioned above, in accordance with the plans and specifications of John Russell Pope and subject to the supervision of his office. We are advised that the George A. Fuller Company are prepared to enter into such a contract and to proceed with the work as soon as this is possible.

"It is estimated that construction and furnishing will require about one year. The contract has been prepared by Mr. Pope's office and approved by my personal attorney as to its legality and as to the bond to be furnished by the construction company. Copies are being furnished to the President, Secretary and Treasurer, and to the Chairman of the Council.

"In my judgment, we have everything to gain and nothing to lose by making the contract *now* and I strongly recommend prompt action."

and the following communication from Chairman Hilton of the Council:

"I have gone over copy of Dr. Dunning's statement you sent me, also copy of the proposed agreement between the A. PH. A. and the George A. Fuller Company, contractors, for erecting the building to be known as the American Institute of Pharmacy. This company is the lowest bidder and also has the reputation of being one of the most responsible builders in the country. I know of nothing that I can suggest to improve same and both Dr. Dunning's letter and the agreement have my approval.

"I feel sure that Mr. John Russell Pope will look after the interests of the ASSOCIATION in every possible way."

(*Motion No. 32*) *It is moved by Dunning that the President, Secretary, and Treasurer of the Association be authorized to enter into a contract with the George A. Fuller Company to erect the Headquarters Building in accordance with the plans and specifications of John Russell Pope, and with provisions for protection mentioned in his letter of April 13, 1932.*

The Chairman of the Council has approved the request of Chairman Dunning for a vote on his motion at the earliest reasonable date and has authorized the calling for a vote at this time. If there is objection or if any member of the Council desires to have additional information or to submit comments, the vote will be considered as tentative.

E. F. KELLY, *Secretary.*

BRIEF NEWS ITEMS FROM MEXICO.

BY G. G. COLIN.

SYNDICATE OF NATIONAL LABORATORIES OF PHARMACEUTICAL PRODUCTS TAKES ACTION TO REPRESS CUT-RATE COMPETITION.

During the month of April, the Syndicate of L. N. P. F. (Laboratorios Nacionales de Productos Farmaceuticos) extended a cordial invitation to the largest manufacturers operating in the City of Mexico to discuss measures that will insure price standardization. At the meeting held at the offices of the Syndicate the following firms attended: Esta-blecimientos Colliere, S. A., Laboratorios "Chinoin," Laboratorios Codex of Carlos Stein & Co., Laboratorios Limousin, S. A. These firms attended as non-members of the Syndicate. The following members were present: Laboratorios "El Aguila," Laboratorio Hipodermico Nacional, Laboratorios Grey, Laboratorios Pravaz, Laboratorios Perez Gil, Laboratorios "Ifusa," Laboratoiro Quimico Central.

President Dr. R. Tervino Garza welcomed the guests and gave an address explaining the motives for this conference and the necessity of standardizing prices. Secretary G. G. Colin then briefly informed those present of the resolutions and discussions held at previous meetings of the Syndicate. All those present offered their coöperation for the purpose.

A committee was appointed to call on other manufacturers who did not attend and who have been following a policy of low prices and long terms, inviting them to coöperate and reconsider their attitude which is detrimental to the industry.

NATIONALISTIC CAMPAIGN BENEFITS DRUG TRADE.

The nationalistic campaign promoted to stimulate consumption of home-made products has been intensified again in view of the excellent results obtained. As a result of this campaign imports have shown a considerable decrease and both the public and physicians are giving preference to products made in this country.

A large building, centrally located, has been adapted to hold exhibits of all manufacturers in the pharmaceutical industry. Suitable entertainment is offered to visitors who are also given samples and literature.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

BALTIMORE.

The members of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION were guests at the Faculty of Pharmacy of the University of Maryland at their recent meeting held April 20, 1932.

Dr. E. V. McCollum, professor of Biochemistry at the School of Hygiene and Public Health, Johns Hopkins University, and international authority on the Sciences of Nutrition and Dietetics, addressed the Branch, and had for his subject.

"OUR PRESENT KNOWLEDGE OF NUTRITION."

Dr. McCollum began with the early researches of Magendie, Liebig, Pettenkofer, Voigt and others, whose work showed that the five fundamental constituents of all foods were proteins, carbohydrates, fats, water and mineral ash, and who demonstrated the necessity of each as a constituent of the diet. Although this work is of inestimable value in that it laid the foundation for the chemical analysis of foods, it also developed the erroneous idea that these components constituted a complete diet and that if one were to eat a sufficient quantity of them he would of a certainty be well nourished.

This idea was definitely disproved by Dr. McCollum in his early researches at the University of Wisconsin, where he fed animals on different experimental diets containing the five components and found that many developed pathologic symptoms and that some died, apparently from inanition. Then began a long and systematic study of foods, having for its purpose the discovery and isolation of any unknown constituents that might be shown to be a necessary factor in the diet. The results of this work, which was begun by Dr. McCollum and is being carried on to-day by a host of workers both here and abroad, have proved fruitful beyond all expectations, and have demonstrated the existence of no less than thirty-seven accessory food factors. Eighteen of these are amino-acids, eleven are chemical elements, one is a carbohydrate, one a fat and six are vitamines. All but the last six are so widely dispersed that if one eats a moderately varied diet he is almost certain to obtain a sufficient quantity of them for bodily needs.

The vitamines differ from other food factors in several respects: they show a definite and relatively limited dispersion among foodstuffs; they occur in extremely small amounts; their absence in the diet proves characteristic pathologic symptoms which are, in most cases, relieved by administration of the appropriate vitamine. It is interesting to note that vitamines, which are necessary to a rugged and vigorous health are found to be most plentiful in raw and natural foods, and in foods that furnish bulk and roughage, rather than those which have been highly purified. Thus leafy vegetables and citrus fruits have a higher vitamin content than fleshy legumes, or potatoes, while polished rice and highly milled flour contain but traces, and sugar, the purest food product known, is utterly devoid of vitamines.

The researches of Dr. McCollum and co-

workers have produced knowledge that is of inestimable value to the health, and therefore to the happiness and prosperity of humanity. Rickets, scurvy and pellagra have fallen before the patient and persistent efforts of the biochemist. Much light has been thrown upon the problems of sterility, dental caries and multiple neuritis. Such contributions transcend a materialistic evaluation; they stand out as beacon lights along the road of human progress.

WM. F. REINDOLLAR,
Secretary-Treasurer.

DETROIT.

The April meeting of the Detroit Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held April 21, 1932, in the Y. M. C. A. Building. The meeting was preceded by a dinner.

L. A. Seltzer, the father of the student night idea, was asked to preside. The minutes of the previous meeting were read and approved. Chairman R. T. Lakey of the Program Committee, outlined the extensive and interesting program arranged by Dean Edward H. Kraus and the University of Michigan for the May meeting and urged a large attendance in Ann Arbor, May 12th.

The students presented a most interesting group of papers as follow

From Detroit College of Pharmacy:

1. Kalman Bator—"Have You Looked at the Label?"
2. Frederick Arnold—"Haliver Oil with Viosterol."
3. Arno Wheeler—"Some Facts about Iodine."
4. James Koich—"Dispensing of Prescriptions."
5. Maurice Kime—"Glass Industry in Pharmacy."
6. Harold Redshaw—"Crystallography."
7. Michael Kovalcik—"Future of Pharmacy."
8. Henry F. Tyszka—"The Fields of Pharmacy."
9. Alfred Lavelli—"Advertising."

From College of the City of Detroit:

1. Miss Eugenia Lemke—"The Early Pharmacist of Detroit."
2. William Briggs—"Apprenticeship and Professional Pharmacy."
3. Ray Poliat—"Beauté de Diable."

Mr. Ingram complimented the students for the splendid papers presented and urged that they be published in the JOURNAL. The outstanding paper was one presented by Miss Eugenia Lemke on "The Early Pharmacist of Detroit." Dean Lakey said much credit is due Miss Lemke for her untiring search through the various libraries in gathering the data for her paper.

Mr. Seltzer said if there was any doubt in the minds of the members as to the wisdom of inviting the pharmacy students into the Detroit Branch, the papers presented by them removed any trace of doubt.

Mr. Seltzer appointed Dean R. T. Lakey of the College of the City of Detroit, Dean Edward H. Kraus of the University of Michigan and Dean E. P. Stout of the Detroit Institute of Technology—to serve on the Committee of Nominations and report at the May meeting, Dean Kraus to act as chairman.

BERNARD A. BIALK, *Secretary.*

UNIVERSITY OF FLORIDA STUDENT BRANCH.

The third meeting of the University of Florida Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in the Chemistry-Pharmacy Building on the evening of February 24th. J. E. Katsch presided.

Chairman H. F. Lynch, of the Program Committee, announced several interesting programs which have been planned for future meetings of the year.

The speaker of the evening was Dean C. E. Mollett of the College of Pharmacy, University of Montana. Dean Mollett is pursuing graduate work under Dr. B. V. Christensen at the University of Florida, and presented a paper on the plant *Coptis occidentalis* with which he did some work this year.

Coptis occidentalis—family Ranunculaceæ (Salisbury) grows abundantly in the mountainous regions of Montana, Oregon and Washington. It is very similar to the official *Coptis trifolia* (N. F. V), but is larger, has long petioled leaves and is 3-flowered.

Dean Mollet showed photographs of the plant and pointed out its botanical relationship to other species of the *Coptis genus.*

The analysis of the plant showed: Coptine—0.31%, berberine—4.6%, resins, traces of starch and total ash—5.3%.

Since this plant is larger, more easily collected, and contains a higher per cent of all the active constituents of the official *Coptis*, Dean

Mollet feels that it will be recognized by the next National Formulary.

The principle use of Coptis is as a simple bitter, but it has been used extensively for various eye-inflammations and as a fluid-glycerite for healing aphthous sores of the mouth.

A large number of the students and faculty of the Pharmacy College were present.

APRIL.

The April meeting of the University of Florida Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in the Chemistry-Pharmacy Building, Monday night, April 27th. James E. Katsch presided.

The treasurer acknowledged receipt of thirty dollars ($30.00) from the AMERICAN PHARMACEUTICAL ASSOCIATION and it was decided that this money be deposited with the Cashier of the University to be withdrawn by the treasurer in such amounts as the Branch will from time to time see fit to use. There was no further business.

President Katsch introduced the Speaker of the evening—Dr. Ouida Davis Abbott, Director of Research, Home Economics Department, University of Florida Experiment Station. Dr. Abbott's talk was on Vitamine "A," with which she has done some work recently.

The term vitamine has been defined as a group name for substances other than fats, carbohydrates, proteins and minerals, which are found in minute quantities in natural foods. They are essential for normal nutrition and for the prevention and cure of various pathological conditions known collectively as "deficiency diseases."

At the present time there are six independent vitamines, whose existence has been definitely proved, and the data are indicating the possibility and probability of at least three more. The known vitamines are vitamines A, B, C, D, E, F and G.

Vitamine A was one of the first vitamines discovered. It is essential for growth and well being of all ages. While it is not the anti-sterility vitamine, it is necessary for reproduction. The absence of this vitamine from the diet produces in experimental animals very definite changes, the most conspicuous of which is condition of the eye known as xerophthalmia, but the most frequent is the abscess at the base of the tongue, and the pus in the sinuses and ears. When vitamine A is low in the diet over a period of time there is an increased susceptibility to bacterial infection, which is supposed to be due to the weakened condition of the tissues. It has been found that the body has the power to store this vitamine and is able to draw on this supply for future use. An abundant supply of vitamine A in early life seems to safeguard the body against later infections as well as provide protection for the present. As growth proceeds the amount of this vitamine must be increased. During pregnancy and lactation there must be a still further increase in the vitamine content of the diet if it is to meet the added demands of these functions.

The chief sources of vitamine A are eggs, liver, milk and butter, thin-leafed green vegetables and the pigmented ones.

Of the four pigments in chlorophyll, *alpha* and *beta* Chlorophyll, xanthophyll and carotin, carotin seems to be the active one. It is from this pigment that the body is able to synthesize vitamine A. Carotin has the formula $C_{40}H_{56}$. Some investigators are of the opinion that there is an enzyme in the kidneys which is able to split carotin, and have proposed the name carotinare for this enzyme.

Slides were shown showing the pathological condition developed in the kidneys, stomach and testes of the rat, resulting from a deficiency of vitamine A.

A. P. MCLEAN, *Secretary.*

NEW YORK.

The April meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the College of Pharmacy, Columbia University, on Monday, the 11th, the chair being taken by Vice-President E. A. Bilhuber. There were 102 persons present.

The minutes of the last meeting were read and approved.

Chairman R. S. Lehman, of the Committee on Education and Legislation, reported that the New York State Legislature had adjourned without passing any of the bills introduced by the New York State Pharmaceutical Association. He referred to the Pharmacy bills before the New Jersey State Legislature and to the forthcoming National Drug Store Survey. He then called attention to an article appearing in the *N. A. R. D. Journal* regarding the labeling of prescriptions entering into Interstate Commerce; the F. I. D. 57 relating to this reads as follows:

"If a package compounded according to a physician's prescription be shipped, sent or transported from any state or territory or the District of Columbia to another state or territory or the District of Columbia by a compounder, druggist, physician or their agents, by mail, express, freight or otherwise, the label upon such package is required to bear the information called for by Congress. If, however, the patient himself, or a member of his household, or the physician himself carries such package across a state line, and such package is not subject to sale, it is held that such package need not be marked so as to conform with the law, because such a transaction is not considered one of interstate commerce. The package may be marked so as to comply with the act by either stamp, pen and ink or typewriter, provided all such written matter is distinctly legible and on the principal label, as prescribed in Regulation 17."

This was discussed by Messers. Lascoff, Raubenheimer and Seley and the report was accepted with a vote of thanks.

Treasurer Currens' report was read and accepted.

Chairman Dr. Miller, of the Membership Committee, submitted the application of Meyer Fineberg for membership in the Branch; the application was approved.

Chairman Schaefer, of the Entertainment Committee for the recent Silver Anniversary Dinner of the Branch to the Delegates of District No. 2, presented a financial report. Treasurer Currens moved that the Secretary be instructed to write letters to the *American Druggist* and the four Colleges of Pharmacy of Greater New York thanking them for their participation in the dinner.

Under the heading of Communications, the Secretary reported that President Fischelis was prevented from being present at this meeting because of legislative matters in New Jersey; the Secretary also stated that he had been asked to announce the meeting of the New York Pharmaceutical Conference at the Hotel Astor on April 19th.

Chairman Ballard,[1] of the Committee on the Progress of Pharmacy, presented an interesting report dealing with many subjects, taken from current pharmaceutical literature; among the topics were: Accident Liability Insurance, with reference to signs, sidewalks, etc.; Removal of Common Stains; Growing Hair; The Return of Show Globes, with formulas for contents; A Veterinarian Pharmacist, operating a pharmacy exclusively for animals; Preparing more uniform and smoother Ointments with Muller and Slab; The Use of Iodine and Sodium Iodide in Radiography; Inclusion of Biology in Pharmaceutical Education in Great Britain.

Dr. Arny then introduced the speaker of the evening, Dr. James C. Munch, director of the Pharmacological Research Laboratories of Sharp & Dohme, and consulting pharmacologist of the U. S. Department of Agriculture. Dr. Arny referred to papers published by Dr. Munch on his research work, saying that he marvelled at such an output from one man.

Dr. Munch's subject was "Recent Advances in the Study of Digitalis and Its Allies." As a general introduction the methods of physiological assay prescribed in U. S. P. X or recommended for U. S. P. XI were very briefly presented. The U. S. P. X method of assay of Digitalis, the so-called "One-Hour Frog Method," was then demonstrated with the assistance of Mr. Arnold Quici. This method consists in selection of frogs weighing between 20 and 30 grams, storing them at a temperature of 15° C. or less until used, the holding at 20° C. for several hours, wiping, weighing and injecting a measured quantity of solution into the ventral lymph sac. The frog is returned to 20° C. water for one hour, then the brain and the spinal cord destroyed and the heart exposed. If too small a quantity of material has been administered the heart will be beating at a normal or slightly decreased rate. If a sufficiently large, or too large, quantity of active material has been injected the heart will be stopped in a characteristic condition; the single ventricle will be tightly contracted, while both auricles are widely dilated, but no muscular contractions will be visible in the heart muscles. By using a large number of frogs under proper conditions, it is pointed out that preparations such as tincture of digitalis might be bioassayed with an accuracy of 10 per cent. To allow for the variability of different lots of frogs, under different conditions of storage, climate, temperature, sex and season, each batch of frogs is standardized simultaneously by the administration of a crystalline standard—ouabain. This ouabain is distributed by the Food

[1] Dr. Ballard is now the Secretary of the Section on Education and Legislation, A. PH. A.

& Drug Administration of the United States Department of Agriculture in accordance with the provisions of the U. S. P. X. Reference was then made to the work being conducted by the Committee on Pharmacology and Bioassay of the AMERICAN PHARMACEUTICAL ASSOCIATION upon the deterioration of tincture of digitalis. For this work approximately 50 gallons of tincture of digitalis were prepared in accordance with the U. S. P X method. A portion of this was diluted with 70% alcohol to constitute a second tincture. Given code letters these two tinctures were stored in flint, amber and blue bottles under various conditions of storage. They have been re-assayed at approximately three-month intervals since their preparation in 1928. This work is being continued to determine the further effects of various factors upon deterioration of tincture of digitalis.

Current research work upon Adonis vernalis was reported, with special reference to investigations by Mercier and Mercier, which suggests that this drug contains two glucosides, one having a diuretic and no cardiac effect, the other cardiac and no diuretic effect. It is reported that the cardiac glucoside is not cumulative in its action. Investigations of authentic samples of the crude drug, as well as commercial lots of fluidextract, have shown that it has the same physiological activity, measured by the U. S. P. X One-Hour Frog Method as does fluidextract of digitalis. Similar investigations on authenticated crude drugs, as well as commercial galenicals, have shown that Apocynum is twice as potent and Convallaria three times as potent as Digitalis. It was accordingly recommended that, if the fluidextract of these products which are now official in N. F. V be recognized in N. F. VI, the following standards be required for bioassay by the One-Hour Frog Method:

Fluidextract of Digitalis.....	0.6 cc. per Kilo
Fluidextract of Adonis.....	0.6 cc. per Kilo
Fluidextract of Apocynum....	0.3 cc. per Kilo
Fluidextract of Convallaria...	0.2 cc. per Kilo

Further investigations were then reported by means of the electrocardiograph which had pointed out the differences, as well as the similarity in action, of the various drugs of the digitalis group. Based upon these animal results clinical investigations are now under contemplation to determine the proper conditions for clinical use of these congeners.

Questions concerning the paper were asked by Drs. Lascoff, Raubenheimer, Nyiri and others. Dr. Wimmer said he felt that all present had enjoyed a most interesting and instructive lecture and he proposed a rising vote of thanks to Dr. Munch; this was carried.

HERBERT C. KASSNER, *Secretary.*

THE ACADEMY OF PHARMACY AND THE NORTHERN OHIO BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The third regular meeting of the Academy of Pharmacy was held in the Biology Lecture Hall of Western Reserve University at 8:00 P.M., Friday, April 8th.

The meeting was called to order by President Flandermeyer. Dean Spease introduced the speaker, Dr. Louis Klein, Director, Medical Service, Parke, Davis and Company.

Dr. Klein discussed "The Present Status of Research in Endocrinology" and presented the following chart as an outline of his talk:

I. Pre-Demonstration Phase: a. Thymus; *b.* Pineal; *c.* Mammary.

II. Demonstration Phase: a. Intestinal hormones—1. Secretin, 2. Cholecystokinin, 3. Duodenal hormone. *b. Placental hormone,* 1. Ovarian-like hormone, 2. Pituitary-like hormones.

III. Concentration Phase: a. Parathyroid, *b.* Corpus luteum—1. Progestational hormone, 2. Relaxative hormone, *c. Anterior Pituitary*—1. Growth hormone, 2. Sex hormone, *d. Testicular hormone, e.* Suprarenal cortex.

IV. Isolation and Analysis Phase: a. Pancreas (Insulin), *b.* Posterior Pituitary—1. Alpha hormone, 2. Beta hormone, *c.* Ovarian follicular hormone—(Theelin) (Theelol).

V. Synthetic Phase: a. Suprarenal medulla (Epinephrine), *b.* Thyroid (Thyroxin), *c.* Theelol converted into Theelin.

Dr. Klein stated that the above chart was a classification of the biochemical problems in endocrinology only from the standpoint of the biochemist. As he explained the chart he pointed out the products which were therapeutically useful and the products that were in the doubtful stages.

The concept of the chart, said Dr. Klein, is rather interesting because from the biochemical standpoint it shows at a glance everything that has been done. The last title is the goal of all

research. Dr. Klein also discussed the compound theelin.

In closing Dr. Klein explained that while he seemed to be a little pessimistic about what had been done in a clinical way in endocrinology, he was very optimistic about what the future will bring out. Within the next few years our notions may be materially changed.

The meeting adjourned after the discussion period.

Bulletin 7 discusses ephedrine solutions regarding dispensing and preservation. *Bulletin 8* relates to Iron preparations.

PHILADELPHIA.

The April meeting of the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Philadelphia College of Pharmacy and Science, on Tuesday evening, April 12, 1932. President Stoneback called the meeting to order.

The minutes of the March meeting were read and approved. Chairman Slothower then proposed the following for membership in the local branch, subject to approval: T. H. Wenke, F. J. Osborne, George Bartholomew, 3d, R. Beresford and J. E. Kramer.

President Stoneback announced the committee appointments for 1932–33, as follows:

Committee on Practical Pharmacy: John Walton, *Chairman;* J. K. Thum, and S. H. Kerlin.

Committee on Professional Relations: W. L. Cliffe, *Chairman;* Dr. Wilmer Krusen, and Dr. John Minehart.

Committee on Membership: Harvey P. Frank, *Chairman;* L. L. Miller, F. R. Firebaugh, Robert Schrey, Alfred Barol, C. G. Bliss and Dr. Frank Eby.

Committee on Entertainment: J. W. E. Harrisson, *Chairman;* Adley B. Nichols, and Raymond Hendrickson.

Because of recent local interest, the drug Cannabis was chosen as the subject for the evening's discussion. President Stoneback introduced the speakers in the following order: Dr. M. S. Dunn, who discussed the Botany and Pharmacognosy of the drug; Dr. C. H. LaWall, who offered interesting information regarding the chemistry and history of Cannabis; Dr. P. S. Pittenger, who described the bioassay, and related personal experiences pertaining to the early attempts at standardization; Dr. J. C. Doane, who presented his observations of persons addicted to Cannabis and other narcotic drugs; and, Mr. Morgan Toehill, who related startling experiences encountered while investigating the misuses of Cannabis.

A general discussion followed, the participants being Messrs. Harrisson, Munch, Dunn, Pittenger and LaWall.

A vote of appreciation wasten dered the speakers by the sixty-five members of the audience.

E. H. MACLAUGHLIN, *Secretary.*

Just before closing forms we are advised of the death of Dr. John R. Minehart, Philadelphia, and of H. L. Meredith, Fort Pierce, Fla., further notice will be given in next issue of the JOURNAL.

To the unprecedented developments of the last half century the medical sciences have contributed their share, and the intense activities of chemists, physicists and bacteriologists in health promotion are reflected in both medicine and pharmacy. In this constant search for facts we naturally see two trends. One of these is the discrediting and disuse of some of the older remedies and methods. The other is the discovery and introduction of the new. This situation is revolutionizing pharmaceutical service in everyone of its phases, but it is not destroying pharmacy itself, for many with ability and understanding have foreseen and are meeting the developments as they arise.—*From an address by E. Fullerton Cook.*

ACTIONS IN CONGRESS ON HEADQUARTERS BUILDING SITE.

Several favorable actions by the District of Columbia on the A. PH. A. Headquarters Building site and the U. S. Senate (Res. No. 50) were taken sometime ago and on May 9th the House acted favorably, which now authorizes Commissioners of the District of Columbia to close upper Water Street between 22nd and 23rd Streets. The Director of Public Buildings and Public Parks of the National Capital is authorized to transfer to the AMERICAN PHARMACEUTICAL ASSOCIATION such an area adjacent to the land owned by the said ASSOCIATION, etc. The further action provides that the design of the said ASSOCIATION's building shall be such as to be approved by the National Commission of Fine Arts and designates its use. On May 10th the message applying was read in the Senate and communicated to the House. The speaker announced his signature to the Joint Resolution. This, it is reasonable to assume, brings the time near when building operations on the American Institute of Pharmacy can be commenced.

EDITORIAL NOTES

Editor: E. G. Eberle, 10 West Chase Street, Baltimore, Md.

Members of the Council, A. PH. A.: S. L. HILTON, *Chairman;* CHARLES H. LAWALL, *Vice-Chairman;* E. F. KELLY, *Secretary;* H. V. ARNY, A. G. DUMEZ, H. A. B. DUNNING, WILLIAM B. DAY, C. E. CASPARI, J. H. BEAL, W. BRUCE PHILIP, T. J. BRADLEY. *Ex-Officio Members:* WALTER D. ADAMS, *President;* J. G. BEARD, J. W. DARGAVEL, *Vice-Presidents;* C. W. HOLTON, *Treasurer;* E. G. EBERLE, *Editor of the Journal;* A. G. DUMEZ, *Editor of the Year Book;* THOMAS ROACH, *Chairman of the House of Delegates.*

Collaborators: The Members of the Council; E. FULLERTON COOK, *Chairman,* U. S. P. Revision Committee; E. N. GATHERCOAL, *Chairman,* N. F. Revision Committee; Chairmen of the Sections, A. PH. A.: L. E. WARREN, C. J. CLAYTON, W. G. CROCKETT, ROWLAND JONES, J. T. LLOYD, TOWNES R. LEIGH, *President,* A. A. C. P.; CHARLES B. JORDAN, *Chairman,* Executive Committee, A. A. C. P.; A. L. I. WINNE, *President,* N. A. B. P.; HENRY C. CHRISTENSEN, *Secretary,* N. A. B. P. Scientific Section—Board of Review on Papers: *Chairman,* GLENN L. JENKINS, Baltimore, Md.; EDWARD E. SWANSON, Indianapolis, Ind.; W. J. HUSA, Gainesville, Fla.

PRESCRIPTION PROBLEMS.

BY S. L. HILTON, PHAR.D.

April 27, 1932

Mr. Juan R. Carandang,
Carandang's Pharmacy,
Tanauan, Batangas,
Phillippine Islands.

Dear Sir:

Yours of March 29th received in regard to precipitation in the formula.

℞

Arrhenal	0.2
Sodium Nucleinate	1.2
Sodium Glycerophosphate	1.5
Iron Glycerophosphate	0.4
Calcium Hypophosphite	1.5
Sodium Hypophosphite	1.25
Sodium Benzoate	2.0
Syrup Sarsaparilla Co.	20.0
Water *q. s. ad*	100.0

Misce:

It would be better to dissolve the iron glycerophosphate in hot water with the addition of 1 cc. of Lactic Acid, U. S. P. Dissolve the calcium and sodium hypophosphites in hot water, mix the two solutions and add the other salts and sufficient lactic acid to make the finished preparation slightly acid, and I think you will overcome the precipitation.

What is Gum Lakol?

℞:

Sodium Salicylate	ʒ iii
Sodium Bicarbonatis	ʒ iii
Sodium Citratis	ʒ iii
Mucilaginis Lakol 1:50	ʒ iii
Tinct. Opii Camphorata	ʒ v
Dist. Water Q. S.	ʒ viii

Misce et sig: ʒ ii in ʒ ii of warm water as rectal injection to be retained.

Mucilage of Lakol is a mucilage prepared from a locust (bean) gum. This gum is also employed for giving body to ice creams and also for surfacing canvas.

INTERNATIONAL PHARMACEUTICAL FEDERATION.

We are in receipt of the following notice and pleased to comply:

We have the honor to inform you that the Board of the Federation has decided to postpone the General Assembly in Prague, which would have been held in September next, to the year 1933.

P. S. We request the editors of the Pharmaceutical Journals to kindly insert this communication.

The Hague, Leyden,
April 6, 1932.

J. J. HOFMAN, *President,*
T. POTJEWIJD, *Secretaire General.*

THE AMERICAN INSTITUTE OF PHARMACY.

The *Baltimore Sun*, "Sunday Magazine Section," of May 1st, had the following to say:

The Pharmacists of the United States have chosen Washington as a headquarters for the AMERICAN PHARMACEUTICAL ASSOCIATION, and soon a handsome building will rise along the western end of the Mall near the Lincoln Memorial and west of the National Academy of Sciences and National Research Council Building. In this structure will be housed a reference library, a historical museum, and a research laboratory—all devoted to the advancement of the profession of pharmacy.

FIFTIETH ANNIVERSARY OF KOCH'S DISCOVERY.

The fiftieth anniversary of Dr. Robert Koch's discovery was celebrated last month, as the announcement of the discovery was made in April of 1882. The number of cases of tuberculosis have been greatly reduced so that this discovery may still be termed one of the major triumphs of bacteriology.

CHEMICAL ELEMENT OF CANCER.

Announcements that the naturally occurring chemical group which is responsible for cell division in cancer as well as in normal tissue has been definitely identified and that cancerous growth in rats has been arrested by the application of the X-ray to the pituitary gland instead of direct to the malignant growth itself were made in Philadelphia before the Federation of American Societies for Experimental Biology.

Dr. Frederick S. Hammett of the research institute of Lankenau Hospital, Philadelphia, who created a mild sensation two years ago with a preliminary statement regarding studies of the sulph-hydryl group, reported that in the interim he had demonstrated unquestionably that the sulph-hydryls were the fundamental chemical element in the growth of the malignant cell.

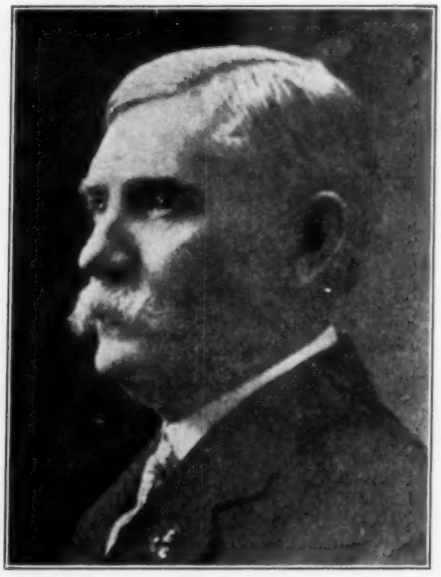
THE AMERICAN PHARMACEUTICAL ASSOCIATION IS CHARTER MEMBER INTER-SOCIETY COLOR COUNCIL.

The AMERICAN PHARMACEUTICAL ASSOCIATION is charter member of the Inter-Society Color Council. E. N. Gathercoal was elected *Chairman* of the Council—for other officers see Roster under "Conferences."

THE FIFTEENTH ANNUAL MEETING OF THE AMERICAN COUNCIL ON EDUCATION.

The 15th annual meeting of the American Council on Education will be held at the Brookings Institution, Washington, May 6th–7th.

Matthias Noll, a veteran member of Kansas Pharmaceutical Association, and for a number of years of the AMERICAN PHARMACEUTICAL ASSOCIATION, has completed the history of Kansas Pharmaceutical Association. The



MATTHIAS NOLL.

work required nearly five years and contains nearly 13 hundred biographical sketches. Besides the history of the Association the book contains historical accounts of the divisions of the drug-trade activities and events in the development of the State.

SECTION ON HISTORICAL PHARMACY.

Chairman L. Gershenfeld is making a strong effort to induce all state pharmaceutical associations to contribute histories of their respective organizations to the Toronto program of the AMERICAN PHARMACEUTICAL ASSOCIATION. See rosters of the Sections on page xii of this issue together with addresses of the officers.

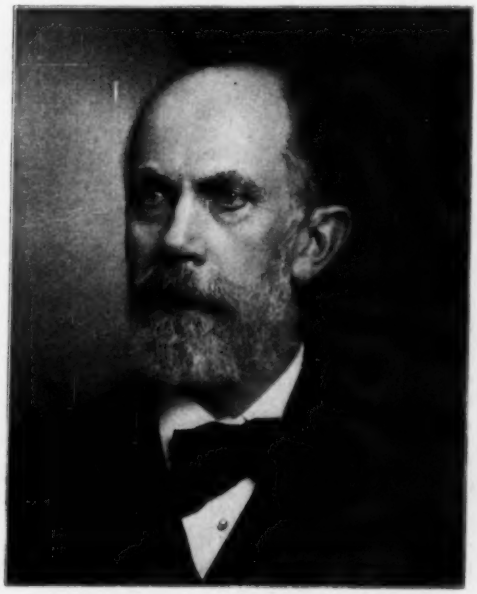
PERSONAL AND NEWS ITEMS.

W. Bruce Philip, President-Elect of the AMERICAN PHARMACEUTICAL ASSOCIATION, will deliver the address to the graduates of the College of Pharmacy of the City of New York, Columbia University, on May 26th. The exercises will be held at the McMillan Academic Theatre, 116th Street and Broadway.

LIFE MEMBERS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

During this year the following have become Life Members of the AMERICAN PHARMACEUTICAL ASSOCIATION (membership of 37 years): Theodore J. Bradley, Boston; Wilhelm Bodemann, Chicago; H. K. Mulford, Philadelphia; Miers Busch, Philadelphia; F. P. Stroup, Philadelphia; Edward A. Hay, Portland, Me.; George D. Rosengarten, Philadelphia.

F. P. STROUP.
A. PH. A. Life Member.



WILHELM BODEMAN.
A. PH. A. Life Member, Veteran and Veteran Organizer.

The medal of the American Institute of Chemists, awarded annually for "noteworthy and outstanding service to the science and profession of chemistry in America," was presented to Dr. Charles H. Herty of New York at a dinner, February 7th, in the Chemists Club.

Dr. Charles H. LaWall, who was appointed some months ago as a member of the International Committee of the Health Council of the League of Nations, to study the subject of opium assay methods, and who was at that time appointed as a Consultant in Pharmaceutical Chemistry to the U. S. Public Health Service of the Treasury Department so that he could legally import the opium upon which the experiments were to be made, has completed the first assignment of the work and sent in his reports to Chairman, Professor, L. Van Itallie of Leyden, Holland.

Instructor Netz gave two illustrated lectures with demonstrations before a group of Minneapolis and other physicians and some pharmacists on April 8th and April 12th; these lectures were supplemental to a course of lectures on prescription writing given previously by Dr. A. D. Hirschfelder. The initial work leading to these two courses was done by the Interprofessional Relations Committee of the Hennepin County Medical Society, the Minneapolis Retail Druggists' Association and the Minneapolis District Dental Society. The College of Pharmacy furnished the prescription materials for the demonstrations.

Carl T. Dyna, our fellow member and hospital pharmacist has been retired by the State of California. Mr. Dyna served for 20 years in

The interior of the remodeled Kapitel-Apotheke zur heiligen Maria, Zagreb (Agram) 1910—had its origin in 1599.

State hospitals and invariably gave importance to pharmacy in these institutions.

Secretary Frank B. Haymaker has issued a *Mother's Day Bulletin* and with it issued the announcement that the Joint Convention of the Virginia Association and West Virginia will be "a whale of a meeting" and shows the whale. Among the speakers will be H. S. Noel, J. H. Beal, H. C. Christensen, W. Bruce Philip and a number of others who are well and favorably known speakers, but not associated with pharmacy.

Charles L. Meyer, Baltimore, sustained a serious fracture of his right arm, the result of a fall.

The last meeting of the Baltimore Retail Druggists was an interesting occasion because of discussions of prescriptions lead by **S. L. Hilton.** A dinner at the Lord Baltimore preceded the program; **Mr. and Mrs. W. Bruce Philip** attended.

John C. Krantz, Jr., and **Glenn L. Jenkins,** on invitation of the Vocational Guidance Bureau, addressed the student body of Forest Park High School last month.

THE KAPITEL PHARMACY AT AGRAM.

The Kapitel Pharmacy of the Holy Mary, located at Agram was founded in 1599. The first apothecary of record is Ivan Petro; Jacob

Front and entrance of Kapitel-Apotheke zur heilige Maria, Zagreb (Agram) 1599–1852.

Gasparini was conductor from 1630–1666, and John Seiczt Ivan from the latter year, other apothecaries of record are Ivan Paukner, Joseph W. Weffort, Ivan Juergens, Alois Ody and, in succession, because of death by various members of the family. The apotheke then passed into the hands of Gracian Mihie, who owned it until 1866 and remodeled the pharmacy; he had placed over the entrance a large oil painting of Mother Mary, by the celebrated artist, Osascy; the latter is still in the pharmacy. After his death the pharmacy was sold to Jean Lapuch, then Rafael Vormastani, J. Cejbek, Karl Kuljak, Anton Ernst Katkic, Ladislav Gayer, Bladimir Bartulic, whose nephew of the same name is still the owner. The latter remodeled the pharmacy; he graduated in pharmacy at Zagrad in 1894 and is a member of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Ground was recently broken for the erection of a research laboratory building at the works of Merck & Co., Inc., at Rahway, N. J. The building will be a Colonial type, brick structure, with a central section 40 ft. by 80 ft., of two stories and basement. On each end of this central section will be two one-story wings, 50 ft. by 100 ft. The wings will be connected with the central section by two one-story units, 10 ft. by 38 ft.

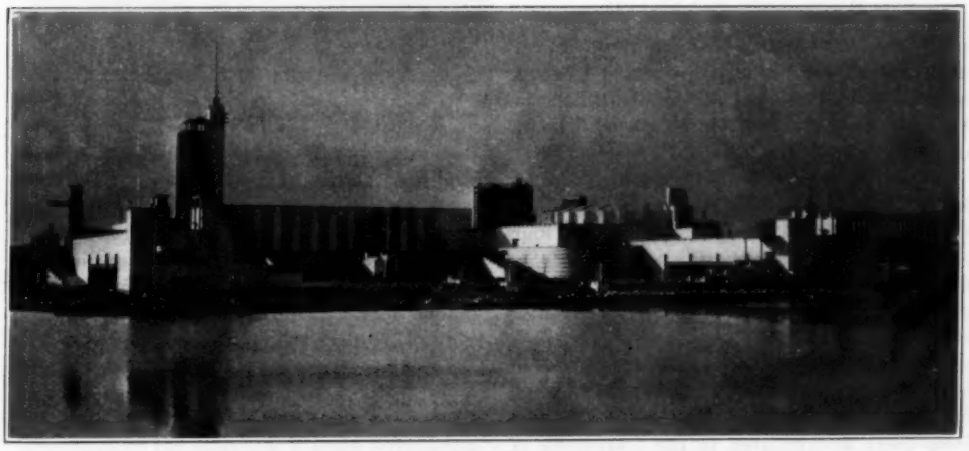
FOURTH INTERNATIONAL CONGRESS OF MEDICINAL AND RELATED PLANTS.

The Fourth International Congress of Medicinal and other plants of the International Federation for the development of medicinal and aromatic plants was held in Paris, July 21st–26th. A very complete report of this meeting has been prepared and printed under the direction of Prof. Emil Perrot, and printed under the direction of the Minister of Agriculture and the Minister of Commerce and Industry, of France, edited by the French National Committee of the Federation, 12 Avenue du Maine, Paris (XV).

The report is an octavo volume of 451 pages in the text and 23 additional pages. A number of illustrations make the report more interesting. The book may be purchased from the department above mentioned; the price is 75 francs and postage additional. There is much in this report of general interest regarding the cultivation of plants and a very interesting account of the Congress, its organization, aims and purposes.

Reports are made by representatives from different countries and each one of these reports is followed by a briefer report in French, and those relating to France, particularly, are more extended.

The frontispiece is a picture of Prof. Dr. Mitlacher, the founder of the Congress. Several of the illustrations are reproductions of photographs of those in attendance at the Congress. Other pictures show the botanical gardens and sections of France through which excursions were made by those in attendance.



Science Hall, Chicago World Fair.—See Editorial.

OBITUARY.

CHARLES WEST PARSONS.

Charles W. Parsons of the scientific staff of E. R. Squibb & Sons and a former editor of The *Practical Druggist*, died in the Hackensack Hospital on April 6th after a brief illness.

He was born in 1861 at Windsor, Conn., and when quite young the family removed to Michigan. There he received his education and graduated from the University of Michigan School of Pharmacy in 1881. Following an appointment as assistant chemist in the Chemical Division of the Department of Agriculture at Washington, he was employed by Schieffelin & Co., New York, and later was editor of the *Druggists Circular* for two years.

In 1883 Mr. Parsons was selected as professor of Analytical Chemistry and Practical Pharmacy in the New York College of Pharmacy. He held this chair until 1888 when he became editor of the *Pharmaceutical Era*. He resigned in 1901 to enter the employ of Smith, Kline & French Co. in Philadelphia. During subsequent years he was connected in turn with E. R. Squibb & Sons, Lehn & Fink, and Hoffmann-La Roche Chemical Works. In 1919 he assumed the editorship of the *American Druggist* and in 1926 returned to E. R. Squibb & Sons.

Mr. Parsons was a member of the AMERICAN PHARMACEUTICAL ASSOCIATION and charter member of the New York Veteran Druggists Association. The funeral services were held April 7th, at his residence in Rutherford, N. J., followed by interment at LeRoy, N. Y.

J. HUNGERFORD SMITH.

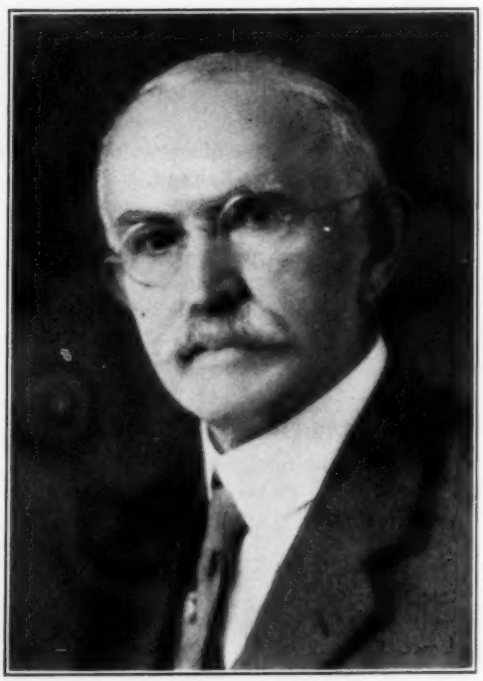
Ill for several years, J. Hungerford Smith, once a small town druggist who developed a nationally known business that was unique in American industry, died April 19th in his home at Rochester, N. Y. He was 77 years old.

Mr. Smith, who organized the J. Hungerford Smith Company, and who served that company as active president until his retirement four years ago due to ill health, was born in Fine, St. Lawrence County, N. Y., on Feb. 20, 1855, the son of the late Col. William P. and Sarah Hungerford Smith.

After receiving his elementary education in his home town, Mr. Smith entered the Hungerford Collegiate Institute at Adams, N. Y., and from there matriculated in the University of Michigan where he was graduated with the degree of pharmaceutical chemist with the class of 1877.

After college, Mr. Smith engaged for a short time as a traveling salesman; in 1880, he established a drug store at Ausable Forks, N. Y., which he conducted successfully for eight years. As a soda fountain was one of the features of his drug store, he made a conscientious effort to serve the best. He applied his natural skill and training in experiments with fruit juices, with the idea of improving the products sold at his own fountain.

His experiments met with almost instant



J. HUNGERFORD SMITH.

success, and there came a demand for his juice mixtures. When the volume of these orders increased to such an extent that he was no longer able to fill them in the limited confines of his drug store, Mr. Smith decided to abandon the drug business and specialize in the then unique field of manufacturing under the name of the J. Hungerford Smith Company.

In 1890, Mr Smith, at the instigation of several Rochester business men, moved his factory to that city. The business was incorporated when it was removed to Rochester, and the factory was enlarged from time to time

until it now occupies more than 250,000 square feet of floor space.

In 1928 Mr. Smith, then 73 years old and having gradually relinquished active participation in the corporation's affairs, retired definitely from business. He continued his membership in the AMERICAN PHARMACEUTICAL ASSOCIATION until his demise.

ROMAINE PIERSON.

Romaine Pierson, owner and publisher of *The Practical Druggist* and of *The Medical Times*, and who had been associated with pharmaceutical and medical publications for more than forty years, died of a sudden heart attack April 27th at his home at 350 Park Avenue, New York City.

Mr. Pierson was sixty-three years old. He was born at Union Springs, N. Y., and was a

ROMAINE PIERSON.

descendant of Abraham Pierson, first president of Yale University. Completing his schooling in the Union Springs public school and in the Friends' Seminary, he entered business in 1888 as a clerk in a retail drug store in his home town. A year later he took employment with Pierson's Pharmacy at Hornwell, N. Y., where he received the most of his pharmaceutical education, and in June 1889, he passed the State board of pharmacy's examination for license as a pharmacist.

In 1891 he started his activities in the publication field, when he gave his spare time to soliciting advertising and subscriptions for *The Druggists Circular*. He entered the employ of the *American Druggist* in 1894 and purchased an interest in the business, becoming secretary of the company later; when the stockholders of the publication purchased the *New York Medical Journal*, later combining it with the *Medical News* and the *Philadelphia Medical Journal*.

"He purchased *The Practical Druggist* from Benjamin Lillard in February 1910, and in December 1911, acquired a controlling interest in *The Medical Times*, a publication then in its fortieth year and which had been partly owned also by Mr. Lillard. In addition to his publication business he was president and manager of Romaine Pierson Advertising Agency, this city.

"Mr. Pierson was a trustee and an elder of the Rutgers Presbyterian Church, this city, member of the Masonic fraternity, and of the Drug and Chemical, New York Athletic, Rumson Country and Lido Country clubs. Funeral services were held April 29th, in the Central Presbyterian Church, Park Avenue, New York City.

"His wife, Mrs. Caroline Robinson Pierson, survives."

WILLIAM L. BUCHER.

William L. Bucher, member of the AMERICAN PHARMACEUTICAL ASSOCIATION, died of bronchial pneumonia, at his home in Columbia, Pa., April 3rd, aged 59 years. The deceased was an alumnus of the Philadelphia College of Pharmacy & Science, class of 1894. He engaged on his own account at Columbia soon after graduation and continued the pharmacy until his death. He held the respect of his fellow-citizens and his pharmacy was known for reliability. He believed in the value of associations and was a member of the local and state pharmaceutical bodies and of the A. PH. A.

Mr. Bucher was a member of the Masonic bodies and other fraternal and business organizations. He was interested in civic affairs, member of the Chamber of Commerce, a director of Columbia Trust Company and other institutions.

Mr. Bucher is survived by his widow, a son, W. L., a senior at Dartmouth, and a daughter. Funeral ceremonies were conducted by the Pastor of the Presbyterian Church, Rev. Guy Wingerd.

SOCIETIES AND COLLEGES.

SECTION ON EDUCATION AND LEGISLATION.

On account of the duties as President of the Conference of Pharmaceutical Secretaries, Charles J. Clayton desired to be relieved of the duties of the secretaryship of the Section on Education and Legislation and Dr. C. W. Ballard consented to accept the duties and has issued the following letter and we hope the members will coöperate with him.

"In order that the work of the Section on Education and Legislation may be up to the standards of previous meetings, the coöperation of all interested in these phases of pharmacy is sought. The fact that this is a joint meeting with the Canadian Pharmaceutical Association makes possible a wider interchange of ideas than has been possible heretofore.

"Research in pharmaceutical education by pharmaceutical educators was the basis of several papers at the Miami meeting and a continuance of this work is earnestly hoped for. Reports on new courses to be offered in connection with the four-year curriculum will be of value. The social aspects of pharmacy school work are deserving of attention. Comment upon legislative activities is always helpful.

"Titles of papers accompanied by short abstracts should be forwarded to the secretary before July first so that the program for the Toronto meeting may be completed promptly."

C. W. BALLARD, *Secretary*,
115 W. 68th St., New York City.

See Roster, page xii, for Section Officers.

AMERICAN DRUG MANUFACTURERS ASSOCIATION.

The 21st annual meeting of the American Drug Manufacturers Association was convened in White Sulphur Springs, West Virginia, April 18th–21st. The list of officers of the Association were reëlected for the ensuing year and are as follows: *President*, Nicholas H. Noyes, Indianapolis; *First Vice-President*, A. Homer Smith, Philadelphia; *Second Vice-President*, A. C. Boylston, St. Louis; *Third Vice-President*, John F. Anderson, New Brunswick, N. J.; *Executive Vice-President* and *Secretary*, Carson P. Frailey, Washington; *Treasurer*, Franklin Black, New York City; *General Council*, Horace W. Bigelow, Detroit.

The Association opposed increase in first-class postage and favored a general sales tax. Tax on dentifrices was opposed.

Greetings from the AMERICAN PHARMACEUTICAL ASSOCIATION were presented by former President Dr. H. A. B. Dunning.

President Noyes in his address referred to the work of the Contact Committee. He stated that its attention had been devoted to assay methods and tolerances touching competitive pharmaceuticals. Much work was done on ergot and these studies resulted in the modification of the U. S. P. text on ergot and fluidextract of ergot being recommended to the U. S. Revision Committee. He said the results of the investigations of the Scientific Section were separately translated into commercial practice. The Biological Section is doing representative work which is recognized by the director of the National Institute of Health.

The President made reference to various meetings that had been held, among them the narcotic convention, and commented on the National Drug Store Survey. The Executive Vice-President and Secretary reported on general activities of the Association.

Secretary E. L. Newcomb of the N. W. D. A. spoke on "Coöperation of the Wholesalers with the Manufacturers."

Dr. H. A. B. Dunning raised a question relative to manufacture and control with the requirements of the A. M. A. Council and those of the U. S. Patent Office.

Dr. F. O. Taylor presided over the sessions of the Scientific Section. It was reported that the members of the Section were actively engaged in pharmacopœial revision work. A number of modifications of tests for organic arsenicals were reviewed and approved.

A lengthy report was made on studies that had been carried on of the vitamines of cod liver oil.

The Pharmaceutical Section was presided over by H. W. Rodehamel.

An extended report was made on "Studies of Ergot and Digitalis," the former by W. J. Rice and the other by F. O. Taylor.

AMERICAN TOILET ARTICLES MANUFACTURERS ASSOCIATION.

The American Manufacturers of Toilet Articles met at the Ambassador Hotel, New York City, April 16th–28th. Taxation was among the more prominent subjects of this meeting.

The officers of last year were reëlected.

LEGAL AND LEGISLATIVE.

ILLICIT DRUG TRAFFIC IN THE FAR EAST.

The Egyptian government's narcotics central bureau, in its report for 1931, shows that Turkey appears to have become an important center of illicit traffic, though the Turkish government is taking steps to deal with the matter. In Greece, again, traffickers are aided by the absence of provisions for the preventive arrest and detention of persons accused. Unfavorable comment is made on the number of cases in which members of certain steamship lines figure as traffickers' agents. The most striking fact of the report is that whereas the number of drug addicts in Egypt decreased considerably last year, the number of traffickers increased. In 1930, 2828 traffickers and 4580 addicts were arrested; in 1931 the numbers were 4327 and 2882.

DRAFT OF A GERMAN LAW REGULATING MEDICINAL PRODUCTS.

A number of existing provisions in the German Medicinal Products law have been recast in a different form, while for other matters, such as the supervision of production and the introduction of a test for certain medicinal products (vaccines, therapeutic and protective serums, arsphenamines, digitalis leaves) new provisions have been drafted.

"One of the important paragraphs contains the regulations concerning the manufacture and sale of medicinal products. The needs of the situation are to be the determining factors in the promulgation of regulations concerning manufacture and sale. It is peculiar that it is not the production of a single preparation that requires authorization but the establishment of a pharmaceutic manufacturing plant. Such authorization may not be given an industrial plant unless the owner furnishes proof that he has the necessary scientific knowledge to carry on such an enterprise in a satisfactory manner. The aim is to eliminate the production of injurious medicaments or such as are likely to deceive the consumer, without imposing more burdens than actually necessary on the manufacture of unobjectionable products. All parties concerned have, on the other hand, an urgent interest in seeing that concessions are conferred only on reliable producers. It is, for example, in no wise desirable that persons without scientific training shall interest themselves in the production of specialties."

It is said that whatever form the law shall assume, it will lead to a clarification of the complicated legal situation in the field of legislation pertaining to medicinal products and will furnish a broad basis for opposing with great energy the illegal traffic in medicinal products and advance the standards of the professions for better medical and pharmaceutical service.

Among the demands are provisions for a responsible, scientifically trained director of a pharmaceutical manufacturing plant; declaration of the active ingredients, holding the producers responsible for the agreement of the declared ingredients with the actual composition, and the abolition of exaggerated or deceptive advertisements.

BOOK NOTICES AND REVIEWS.

Colloid Aspects of Foods, Chemistry and Technology. By WILLIAM CLAYTON, D.Sc. (Liverpool), F.I.C. VII + 571 pages, with 64 illustrations. P. Blakiston's Son & Co., Inc., 1932.

In the preface the author states his reason for presenting this book and the function which he expects it to fulfil as follows:

"Whilst there are several textbooks available in English, German and French which deal with the organic chemistry of foods, the chemical aspects of nutrition and with food analysis, no attempt seems to have been made to survey the field in relation to those physico-chemical aspects of food chemistry which come within the range of modern colloid chemistry. The present volume seeks to fill this gap in the textbook literature."

"It is not a treatise on food technology, but rather an introductory guide to those aspects and problems of a colloid nature which may be unfamiliar to the food chemist who has not specialized in colloid chemistry and physics."

On the whole it may be said that the author has achieved what he set out to accomplish; but before discussing the book in somewhat greater detail, it will be instructive to review briefly the historical background of modern colloid chemistry. Colloid substances, as we now call them, are not at all new to mankind,

though colloid chemistry is one of the newly recognized branches of chemical science. In general properties, most of mankind's basic foodstuffs, clothing materials and structural elements are still much the same as those known to the ancients. In fact, except as Nature offered certain minerals, the early civilizations were more familiar with colloid, or at least amorphous materials than with crystalline. However, the realization that a crystalline condition was indicative of a high degree of purity made the crystallization of compounds one of the fundamentals of chemistry. The early advances of modern chemistry were based largely on the study of crystalline, that is purified, substances. The generalizations deduced therefrom naturally pertained to these crystalline materials and a distinction was gradually built up between the better understood crystalline group and the less well understood amorphous materials which seemed to defy crystallization (*i. e.*, purification). Attendant upon the description of the preparation and chemical reactions of crystalline compounds there was assembled an ever-growing mass of data pertaining to their physical properties. Thus physical chemistry had its inception and development. Not content with studying crystalline compounds alone, physical chemists extended their inquiries to amorphous bodies as well. So it came about that Graham, inspired by his observations on diffusion, classified all substances as crystalloid or colloid because the structural differences coincided roughly with the extremes in this physical property. The acceptance of Graham's classification led in time to the development of colloid chemistry, which is really a branch of physical chemistry.

While the organic chemist has been relatively slow in unraveling the structure of colloids, owing to the inherent difficulty in purifying, *i. e.*, crystallizing, these materials, the physical chemist has forged ahead with an ambitious program to explain the particular behavior of colloids through the study of their physical properties. Hence Clayton's book is essentially a summary of physical properties of foodstuffs, consisting of a collection of descriptive essays on selected materials or processes. These include: the scope of colloid chemistry; agar-agar and gums; the chemistry of the proteins; gelatin; colloids in cereal chemistry; emulsions; the colloid chemistry of milk and milk products; colloid aspects of nutritional chemistry; colloid problems in sugar technology; fruit jellies, jams and marmalades; colloid phenomena in brewing; the freezing and thawing of colloid systems; the treatment of water and factory effluents. Supplementing the text are a glossary of terms, a bibliography of more than 2000 references, author and subject indices. The treatment of these subjects is largely narrative and descriptive; the style is simple, direct and very readable. Numerous tables, graphs and illustrations facilitate a ready comprehension of the subject matter. Of the mathematical discussions, few involve directly the concepts of the calculus.

With the exception of the chapter on freezing, there appears to be almost no treatment of the colloid chemistry of foodstuffs from the standpoint of a common phenomenon. Gelatin swells, casein precipitates or causes distress to an infant by the nature of its curd, flour is baked to bread, beer foams, sugar does not crystallize perfectly unless the colloids are refined out or the color absorbed by active carbons. That is, each colloid has been studied largely with respect to some distinctive or technologically inportant property rather than as a member of a group possessing generalized properties. Which means, with all due respect for the brilliant achievements of the colloid chemists, that the study of the physical properties of colloids has not proved an open sesame for all the difficulties in this field. Much interesting and valuable information has been assembled. But here, as elsewhere in chemical science, a really complete description is not possible until physical and structural knowledge is balanced. The reviewer is disappointed that more effort was not devoted to discussing foodstuffs generally, according to specific physical properties in addition to the reverse classification. The fault, if such it be, of course does not rest solely with the author. The science of colloid chemistry is still too recent in origin to have permitted the recording of all the data necessary to complete such discussions.

As regards the pharmaceutical profession, this book will ordinarily not interest the retailer. Students, teachers or manufacturers will be more likely to profit. To them the book is recommended for its dispassionate description of the present status of researches and technology in food chemistry and for the numerous suggestions for the study of pharmaceuticals which will surely be forthcoming from a perusal of its pages.—ROLAND E. KREMERS.